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UNIPOLAR ELECTROCARDIOGRAPHIC LEADS

EFFECTS PRODUCED BY ELIMINATING THE RESISTORS BETWEEN THE LIMB ELECTRODES AND THE CENTRAL TERMINAL*

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INTRODUCTION

IN 1934, Wilson, Johnston, Macleod, and Barker[1] described a method of obtaining electrocardiograms that represent the potential variations of a single electrode. In this method an exploring electrode is paired with a central terminal connected to electrodes on the right arm, left arm, and left leg through three equal noninductive resistances. It was recommended that these resistances be made large in comparison with the largest body-resistance in any of the three standard limb leads, and it was pointed out that they could be considered adequately large when the deflections in these leads were not significantly altered by connecting the central terminal to the limb electrodes. In the earliest experiments resistors of 25,000 ohms were employed, but these were later replaced by resistors of 5,000 ohms in order to reduce distortion of the tracings due to stray 60 cycle current.

In 1942, Goldberger[2] introduced a modification of this method in which the resistors between the central terminal and the limb electrodes are eliminated. In a series of cases he compared the deflections of the precordial and the unipolar

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limb leads taken with a central terminal connected directly to these electrodes with those of the same leads taken in accordance with the original technique, and was not able to detect any significant difference between them. It may be mentioned incidentally that soon after unipolar precordial leads began to be used regularly in this laboratory, Dr. F. D. Johnston took a considerable number of tracings in the manner afterward advocated by Goldberger. Cursory examination of these records did not disclose any striking difference between them and those taken with resistors. At that time, however, it seemed advisable to adopt a single standard technique for taking precordial electrocardiograms, and it was felt that the use of resistors should not be given up until an exhaustive investigation had shown that they were unnecessary.

Goldberger's method has now come into widespread use, and it seemed desirable to have more exact information bearing upon the question as to whether the insertion of resistors in the arms of the central terminal serves any useful purpose. The potential variations of the precordium are large in comparison with those of the extremities and it is not to be expected that the presence or size of such resistors will have very conspicuous effects upon the amplitude or form of the larger deflections of the precordial electrocardiogram. Taking precordial tracings by both of the methods in question and comparing them did not, therefore, seem to us to be a particularly advantageous way of securing the data required. For this reason, as well as others, we adopted a different plan.

METHOD AND OBSERVATIONS

In a series of 500 consecutive routine electrocardiographic examinations, the electrode on the left arm was paired with a central terminal connected to electrodes on the right arm and left leg through equal resistances of 5,000 ohms. As soon as this lead had been taken, the electrodes on the right arm and left leg were connected together by means of a short length of copper wire with a clip on each end, and a second record was made. This technique made it possible to take the two records to be compared in quick succession and thus eliminate variations in "contact" or "skin" resistance, such as are likely to take place with the lapse of time. The records were taken by the electrocardiographic technicians in the course of their regular work and any conclusions based upon them are, therefore, applicable to routine clinical electrocardiograms.

In each of the 1,000 tracings the deflection produced by throwing 1.0 millivolt into the circuit and the amplitudes of the P,Q,R,S, and T deflections were measured to the nearest two-tenths of a millimeter. After appropriate corrections for errors in standardization had been made, the corresponding deflections of each pair of records were compared with the following results:

P Wave.—In twenty-nine instances (5.8 per cent) there was a conspicuous difference in the auricular complex between the records taken by the two different methods. In some instances the P wave was isoelectric in one tracing and upright or inverted in the other; in other instances this deflection was upright in one tracing and inverted in its fellow (Fig. 1, Tracings *1*,*2*,*3*,*9*, and *17*).

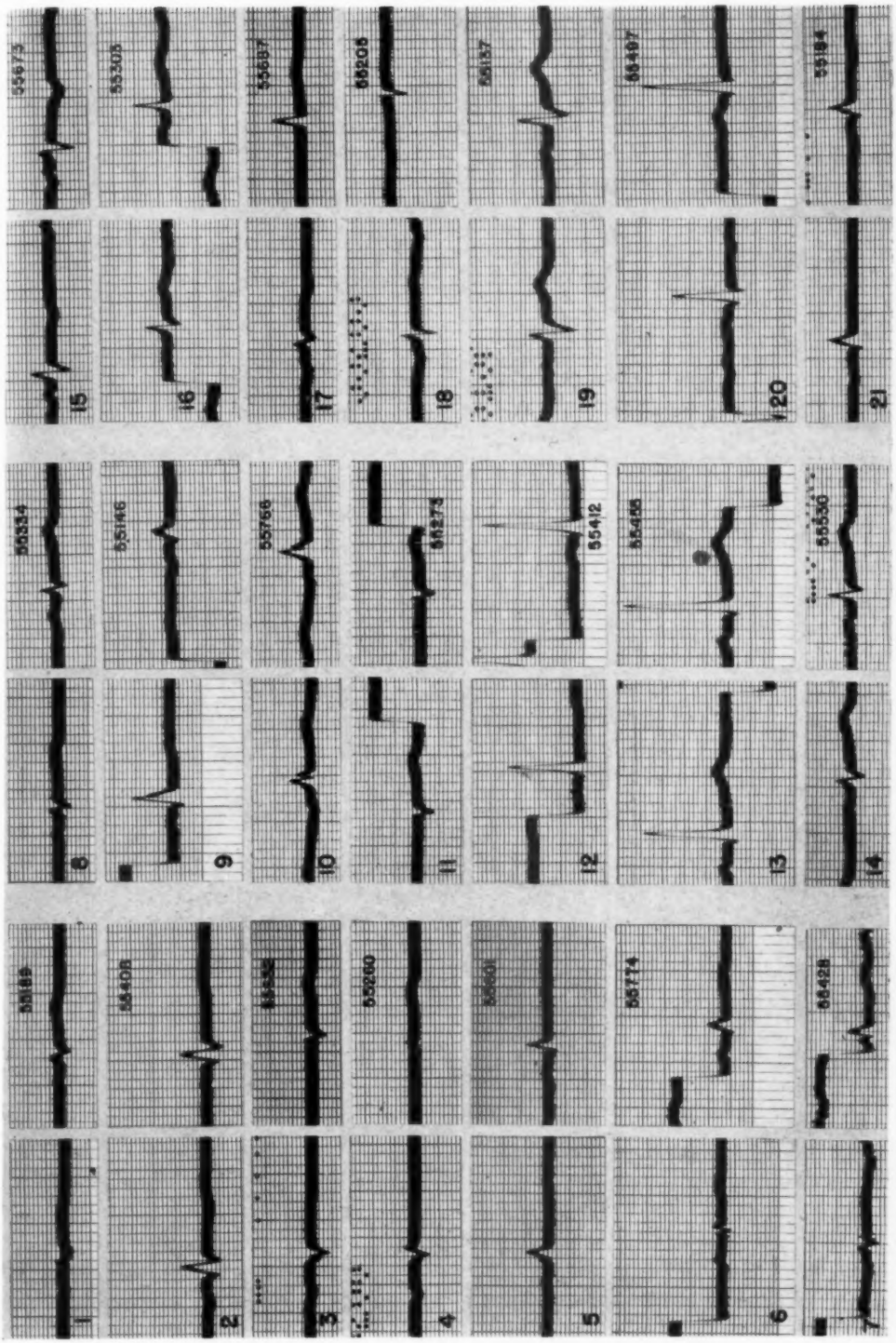

Fig. 1.—Leads from the left arm taken with a central terminal connected to electrodes on the right arm and left leg through resistances of 5,000 ohms. The first tracing of each pair was taken before, the second after, these electrodes were connected together by means of a short length of copper wire.

Q Wave.—This deflection was absent in one record and present in the other in eight instances (1.6 per cent). Tracings 3 through 6 of Fig. 1 show the most striking differences encountered.

R Wave.—A difference of 2 to 7 mm. in the height of the R deflection occurred in fifty cases (10 per cent). See Tracings 6 through 20 of Fig. 1.

S Wave.—This deflection was present in one tracing and absent in the other in five instances (1 per cent). See Tracings 16 and 17 of Fig. 1. In twenty-eight additional cases (5.6 per cent), it was at least twice as large in one record of the pair as in the other.

T Wave.—This component was upright in one tracing and inverted in the other or isoelectric in one tracing and not in the other in twelve cases (2.4 per cent). See Tracings 3, 4, 6, 20, and 21 of Fig. 1. In thirty-two additional cases (6.4 per cent), it was at least twice as large in one record as in the other.

DISCUSSION

These observations indicate that under conditions such as obtain in the taking of routine clinical records, a central terminal connected to the limb electrodes through large resistances may be expected to yield results significantly different from those obtained with a central terminal connected directly to these electrodes in about one case out of ten. Why should the elimination of the resistors in the arms of the central terminal have striking effects in some cases and not in others? Are the results of eliminating these resistors predictable? Is it possible to estimate the maximal change in the potential of the central terminal that this procedure can produce? We shall not undertake here to offer complete and final answers to these questions, but it seems desirable to call attention to some of the factors that have an important bearing upon them.

Connecting electrodes on the extremities to a central terminal completes circuits previously open and establishes currents which did not exist before. These currents are necessarily accompanied by a voltage drop across each of the circuit elements through which they flow. Among these circuit elements are the resistances in the arms of the central terminal, the resistances at the surfaces of the electrodes, the resistances of the areas of skin beneath the electrodes, and the resistances of the internal tissues of the extremities and of the trunk. If the electrodes are small in comparison with the magnitudes of the currents set up, the current densities over their surfaces will be large and the voltage drops at these surfaces and across the underlying skin may be significantly affected by polarization.[3]

It is evident, therefore, that the potentials of the limb electrodes before and their potentials after they are connected to the central terminal must always differ in some degree, and under some circumstances, may differ greatly and in an unpredictable manner. It is also clearly desirable that leads in which the central terminal serves as the reference electrode shall not be less trustworthy than the standard limb leads; that is to say, that the results which they yield shall not be dependent upon the personal equation of the person who uses them or upon purely extrinsic circumstances which he cannot take account of or modify.

Of the circuit elements mentioned, the resistances in the arms of the central terminal, at the surfaces of the electrodes, and in the skin are either completely or to a large extent under our control. Making the first as large as is practicable will reduce the currents set up by connecting the limb electrodes to the central terminal to their lowest possible values and thus greatly diminish the likelihood of significant polarization and the magnitude of the alterations in the potential differences inside the body and at its surface produced by this procedure. The limb electrodes should be relatively large also, for the densities of the currents through their surfaces and the underlying skin, and consequently the "contact" and skin resistances and the magnitude of any polarization that may occur, will vary inversely with their size. The skin resistances can be diminished by proper preparation of the skin, and the lower these resistances, the smaller the chance that they will be grossly unequal or constitute large fractions of the total resistances in the circuits of which they are a part.

The simple equations which express the potentials, V_R, V_L, and V_F, of the apices of Einthoven's triangle in terms of the deflections in the standard limb leads were originally based upon the conclusion that the sum of the potentials of these apices is zero for all positions of the electrical axis of the heart. This conclusion may or may not be valid. In either case, these equations give the potentials of the right arm, left arm, and left leg with respect to their mean as the reference level. Take for example the equation for the potential of the left leg in terms of the deflections in Leads II and III. We have

$$(1)\quad \frac{II + III}{3} = \frac{2V_F - V_R - V_L}{3} = V_F - \left(\frac{V_F + V_R + V_L}{3}\right)$$

The last expression is obtained from the second by first adding and then subtracting V_F.

What exactly do the expressions V_R, V_L, and V_F in these equations represent? That clearly depends upon what the deflections in the limb leads represent. It was shown long ago[4,5] that when the standard limb leads are properly taken one at a time in the usual way, the deflections recorded represent the potential differences between the limb electrodes that would have existed if they had not been attached to the terminals of the electrocardiograph. The principle upon which this surprising conclusion depends is one that was discovered by Helmholtz[6] as long ago as 1853. We conclude, therefore, that the symbols in question represent the potentials of the limb electrodes before they have been brought into contact with any conductor other than the body.

It is then clearly possible to compute the potentials of the limb electrodes with respect to their mean when the deflections in the limb leads are known. The values so obtained may be considered the potentials of these electrodes with respect to an "ideal" central terminal joined to them by infinite resistances. It is also possible, by a procedure analagous to that devised by Einthoven, Bergansius, and Bijtel[4] for another purpose, to construct a central terminal which will have the same potential as an "ideal" terminal of this kind. They showed that by employing three string galvanometers it is possible to take the three limb

leads simultaneously and still obtain accurately standardized records, provided that the resistances in the three circuits are equalized and the sensitivities of the three galvanometers are properly standardized.

We can in the same way adjust the value of the resistances in the three arms of the central terminal in such a way as to make the total resistances in the circuits which include the body equal. The procedure required is the same as that employed by Einthoven and his associates[4] and the example discussed by them is equally suitable for the present purpose. Fig. 2 is reproduced from their paper. The measured body resistances in Leads I, II, and III are given as a, $a + p$, and $a + p + q$, respectively. It is required to determine x, the resistance that must be attached to the right arm electrode, and the resistance y that must be attached to the left arm electrode in order to equalize the resistances in the three limb leads. If we represent the resistances associated with the contacts on the right arm, left arm, and left leg by R_r, R_l, and R_f, respectively, the equalized resistances in three leads will be represented by the following equation:

$$(2) \quad R_r + R_l = a + x + y = R_r + R_f = a + p + x = R_l + R_f = a + p + q + y$$

Solving for x and y, we get x equals $p + q$ and y equals p.

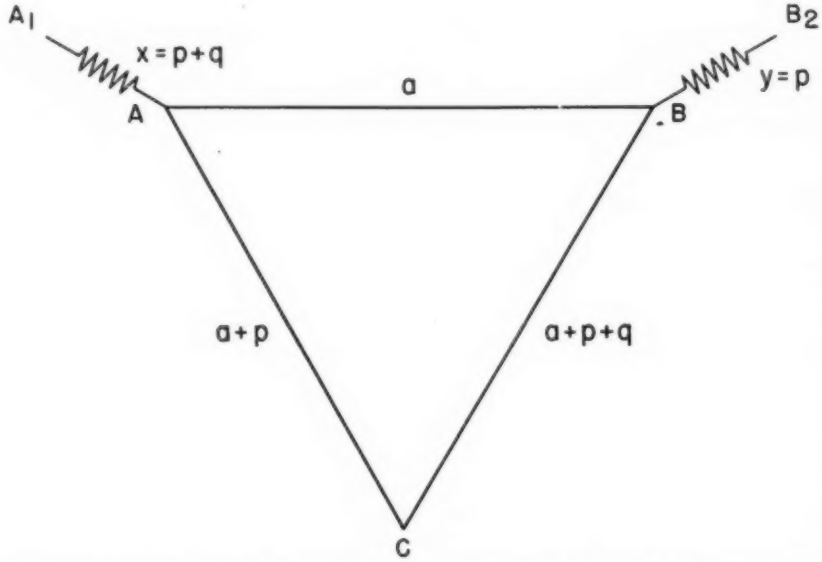

Fig. 2.—Diagram showing method of equalizing the resistances in the limb leads. Reproduced with minor changes from an article by Einthoven, Bergansius, and Bijtel.[4]

A central terminal joined to the right arm electrode (A of Fig. 2) by a resistance R plus x, to the left arm electrode (B) by a resistance R plus y, and to the left leg electrode (C) by a resistance R, will be separated from the points labeled A_1, B_2, and C in Fig. 2 by equal resistances of R ohms. The total resistances in the circuits of which these equal resistances are corresponding elements are equal. Each of the three potential differences between the central terminal and the points A_1, B_2, and C is proportional to, and represents the same fraction

of, the total drop in voltage, or electromotive force, in the circuit to which it belongs. The relations which these statements express are not dependent upon the magnitude of the equal resistances of R ohms. If these resistances are increased step by step, the fraction of the total drop in voltage in each of the circuits corresponding to the potential differences specified will become larger and larger. The limits approached by these potential differences as the value of R becomes infinite are clearly the potentials of the limb electrodes (with respect to their mean) before they were connected to the central terminal. It is easily shown, however, that under the circumstances postulated, the potential of the central terminal is not altered by changing the size of the equal resistors between it and the points A_1, B_2, and C. The sum of the voltage drops across these equal resistors is zero and their relative magnitudes are constant. For very large values of the resistors we have, therefore,

$$(3)\quad (V_R - V_T) + (V_L - V_T) + (V_F - V_T) = O \qquad V_T = \frac{V_R + V_L + V_F}{3}$$

For any other value of the resistors, we have

$$(4)\quad K(V_R - V_T) + K(V_L - V_T) + K(V_F - V_T) = O \qquad V_T = \frac{V_R + V_L + V_F}{3}$$

where K is a fraction equal to R divided by the total resistance in each of the circuits of which the three resistors of R ohms are corresponding elements.

The various circuit elements involved in problems of the kind under consideration are shown diagrammatically in Fig. 3. In this figure E_1, E_2, and E_3

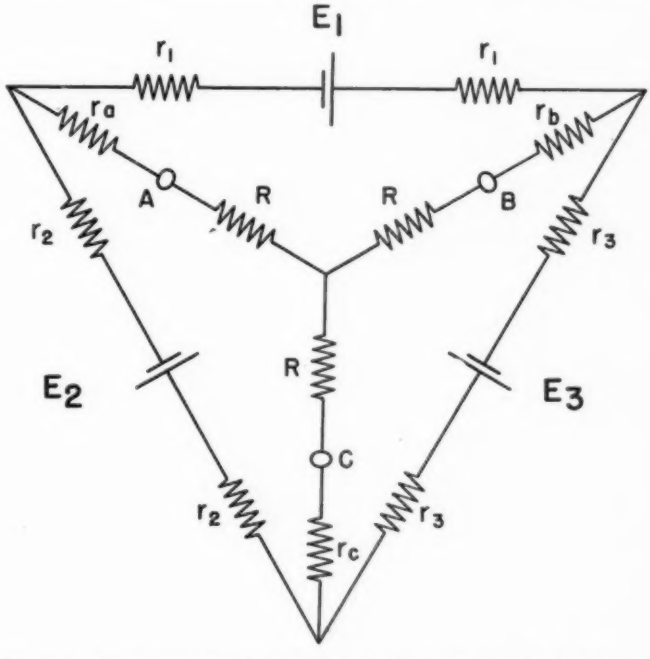

Fig. 3.—Diagram showing the circuit elements of the circuits established by connection of the limb electrodes to a central terminal. See text.

represent the open circuit voltages in the three limb leads, and the small circles (A, B, and C) are the limb electrodes. The body resistances are divided into two fractions. The resistances, across which there is a flow of current only when the limb electrodes are connected one to another by an external conductor, are indicated by the symbols r_a, r_b, and r_c. The other body resistances are labeled r_1, r_2, and r_3. The letter R refers to the equal resistances in the arms of the central terminal. The resistances, r_1, r_2, and r_3, of the tissues of the trunk and those parts of the extremities adjacent to the trunk, through which there is a flow of current before the limb electrodes are joined to any external conductor, are presumably small and approximately equal. On the other hand, the "contact" and skin resistances, which constitute the greater part of r_a, r_b, and r_c, are probably relatively large and frequently unequal.[3]

The following conclusions require no further explanation. When the differences in magnitude between the resistances in the limb leads are small in comparison with R, the potential of the central terminal is the mean of the open circuit potentials of the limb electrodes. When the resistances R are large in comparison with the resistances in the limb leads, the deflections of the leads from the central terminal to the limb electrodes represent the open circuit potentials of these electrodes with respect to their mean. When the resistances R are not large and one of the resistances r_a, r_b, and r_c is much smaller than the other two, the potential of the central terminal will fluctuate in unison with that of the corresponding limb electrode unless the potential variations of this electrode happen to be small in comparison to those of its fellows. When R is not large in comparison with the resistances in the limb leads and r_a, r_b, and r_c are equal, the voltage drops across the resistances R will represent only a fraction of the open circuit potentials of the limb electrodes.

When the value of R is zero, all of the limb electrodes are at the same potential. If the resistances in the limb leads are equal, this potential will be the mean of the open circuit potentials of these electrodes. If r_a, r_b, and r_c are unequal, the potential of the short-circuited limb electrodes will reflect the potential fluctuations of the limb electrode corresponding to the smallest of these resistances. If a central terminal directly connected to the limb electrodes is paired with an exploring electrode, and this electrode is placed on one of the extremities distal to the electrode which is connected to the central terminal, the record obtained will represent the fluctuations of the voltage drop across the skin under the latter. This voltage drop will be proportional to the open circuit potential of the extremity only in case the resistances in the limb leads are precisely equal.

When the resistances R are so large in comparison with the resistances in the limb leads that the voltage drops in the arms of the central terminal are approximately equal to the open circuit potentials of the limb electrodes with respect to their mean, the augmented unipolar limb leads introduced by Goldberger will yield deflections of the same form as, but 50 per cent larger than, the deflections of the corresponding unaugmented leads. This is obviously not the case when R is small, for then the unaugmented leads will record only a small and the augmented leads a large fraction of the open circuit potential variations of the limb

electrodes. When R is zero, the unaugmented leads record nothing. When augmented unipolar leads are taken with a central terminal connected directly to two limb electrodes (R zero), the results are likely to be greatly influenced by the relative magnitude of the two skin resistances involved. The potential of the central terminal, under these circumstances, will not be the mean of the open circuit potentials of the limbs to which it is attached unless these skin resistances are equal.

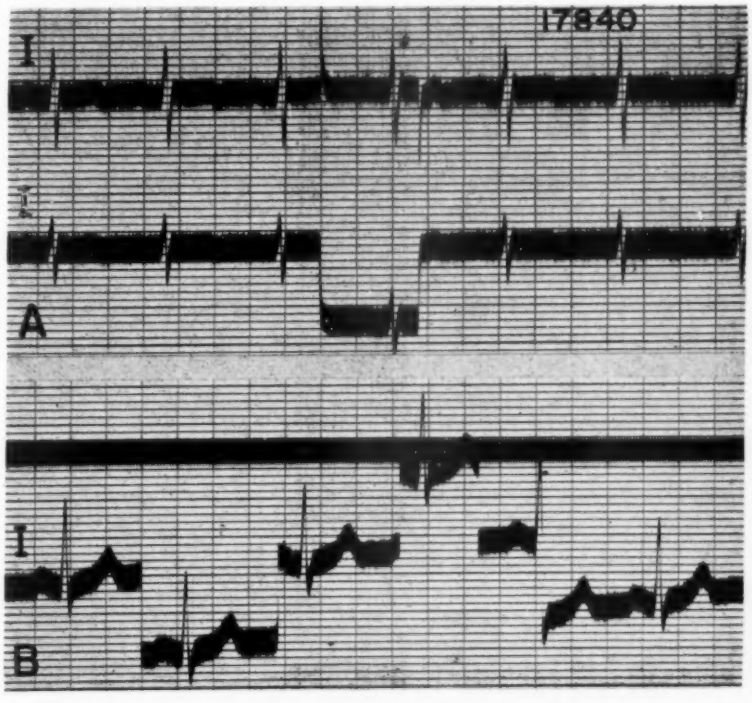

Fig. 4.—*A*, Lead II taken simultaneously with two string galvanometers from a single pair of needle electrodes in the subject's right arm and left leg. The upper record was taken without and the lower record with a single-stage direct current vacuum tube amplifier in the circuit.

B, Record taken with the galvanometer, having the vacuum tube in the circuit, after the other galvanometer had been disconnected from the electrodes.

It may be worth while to give an illustration of the effect on the form of the electrocardiogram produced by polarization in a circuit of relatively low resistance. The tracings shown in Fig. 4 were obtained in the following way. Small steel needles thrust through the skin of the two arms were substituted for the usual limb electrodes and two records of Lead I were taken simultaneously with two coupled string galvanometers. The same electrodes were connected to both galvanometers; to *one* in the usual way and to the other through a single-stage direct current amplifier.[1] The external resistance in the first circuit was then the relatively low resistance of the galvanometer string (about 2,000 ohms), whereas that in the second circuit was the extremely high input resistance of a

vacuum tube. When 1.0 millivolt was thrown into the two circuits, they behaved very differently; the high-resistance circuit yielded a sustained deflection of approximately 1.0 cm. (Fig. 4,*A*). The low-resistance circuit, however, displayed a sharp upward deflection of short duration when the test voltage was thrown in and a similar downward deflection when it was thrown out. On the other hand, the deflections of the two electrocardiographic tracings are identical in form, although different in size. After this record had been taken, the low-resistance circuit was broken and it will be noted that the effect upon the tracing obtained with the high-resistance circuit was profound (Fig. 4,*B*).

We have no evidence bearing on the question as to whether polarization does or does not commonly occur in the low-resistance circuits established when the central terminal is connected directly to the limb electrodes. Nor do we know whether the effects produced by short-circuiting the right arm and left leg electrodes, which are illustrated in Fig. 1, were due chiefly to polarization or chiefly to inequalities of the skin resistances involved. It should be noted that when the standard limb leads are taken with a low-resistance electrocardiograph, the presence of polarization can be easily recognized by the effect which it has upon the deflection produced when a standardizing voltage is thrown into the circuit (Fig. 4). On the other hand, polarization resulting from the flow of current set up by connecting the central terminal to the limb electrodes cannot be easily detected. Polarization arising in this way will distort the tracings obtained through its effect upon the potential of the central terminal; it will not distort the deflection produced by throwing a test voltage into the galvanometer circuit while taking a lead from the central terminal to some other point. It seems essential, therefore, that the resistances in arms of the central terminal be large. Einthoven and Bijtel,[3] who made an exhaustive study of the resistance, electrostatic capacity, and polarization capacity of the skin and their effects upon records taken with the string galvanometer, expressed the opinion that when the external resistance in the galvanometer circuit was 10,000 ohms or more the tracings obtained would not be significantly distorted, provided that the skin resistance had been reduced by the use of 20 per cent sodium chloride solution. At that time the electrodes commonly used were of the immersion type.

CONCLUSIONS

The potential of a central terminal connected to the limb electrodes through resistors of 5,000 ohms and the potential of a central terminal connected directly to these electrodes without intervening resistors may be expected to differ significantly in about one case out of ten.

The resistances in the arms of the central terminal should be large in comparison with the body resistances in the limb leads.

When the resistances in the arms of the central terminal are eliminated, its potential is determined by the relative magnitudes of the resistances of the areas of skin underlying the electrodes to which it is attached and possibly, to some extent, by the effects of polarization.

APPENDIX

A. The Currents in the Arms of the Central Terminal.—

Let i_1, i_2, and i_3 represent the counterclockwise currents in the three loops of the network shown in Fig. 3, containing the resistances r_1, r_2, and r_3, respectively. By Kirchhoff's voltage law we have then the three equations:

$$\begin{aligned} r_1 i_1 + R_b(i_1 - i_3) + R_a(i_1 - i_2) &= E_1 \\ r_2 i_2 + R_a(i_2 - i_1) + R_c(i_2 - i_3) &= -E_2 \\ r_3 i_3 + R_c(i_3 - i_2) + R_b(i_3 - i_1) &= E_3 \end{aligned}$$

The symbols R_a, R_b, and R_c are here used to represent (r_a+R), (r_b+R), and (r_c+R), respectively. These three equations can be solved for i_1, i_2, and i_3. The expressions for i_a, i_b, and i_c, the currents flowing toward the central terminal through its three branches, may then be computed by means of the relations; i_a equals i_2 minus i_1; i_b equals i_1 minus i_3; and i_c equals i_3 minus i_2.

In this way we obtain

$$i_c = \frac{[r_1 r_3 + (r_1 + r_2 + r_3) R_b] E_2 + [r_1 r_2 + (r_1 + r_2 + r_3) R_a] E_3}{r_1 r_2 r_3 + r_1 r_2 (R_b + R_c) + r_1 r_3 (R_a + R_c) + r_2 r_3 (R_a + R_b) \ (r_1 + r_2 + r_3)(R_a R_b + R_a R_c + R_b R_c)}$$

For i_a and i_b, the denominator is the same and the numerators are, respectively:

$$-[r_2 r_3 + (r_1 + r_2 + r_3) R_c] E_1 - [r_1 r_3 + (r_1 + r_2 + r_3) R_b] E_2 \text{ and}$$
$$[r_2 r_3 + (r_1 + r_2 + r_3) R_c] E_1 - [r_1 r_2 + (r_1 + r_2 + r_3) R_a] E_3.$$

When the resistances r_2 and r_3 are equal to r_1, the expression toward the central terminal from the leg electrode is

$$i_c = \frac{(r_1 + 3R_b) E_2 + (r_1 + 3R_a) E_3}{(r_1)^2 + 2r_1(R_a + R_b + R_c) + 3(R_a R_b + R_a R_c + R_b R_c)}$$

and when, in addition, the resistances R_a and R_b are equal to R_c, we have $i_c = \dfrac{E_2 + E_3}{r_1 + 3R_c}$

B. The Potential of the Central Terminal.—

When the resistances R_a, R_b, and R_c are equal, the potential of the central terminal is the mean of the potentials of the three extremity electrodes:

$$V_T = (1/3)(V_R + V_L + V_F)$$

When these resistances are unequal, the potential of the central terminal V_T' may be obtained as follows:

We have the equations:

$$\begin{aligned} (1/R_a)(V_R - V_T') &= i_a \\ (1/R_b)(V_L - V_T') &= i_b \\ (1/R_c)(V_F - V_T') &= i_c \end{aligned}$$

By Kirchhoff's current law the sum of the currents i_a, i_b, and i_c is zero. Consequently,

$$V_T' = \frac{R_b R_c V_R + R_a R_c V_L + R_a R_b R_F}{R_a R_b + R_a R_c + R_b R_c}$$

and

$$V_T' - V_T = \frac{R_b R_c V_R + R_a R_c V_L + R_a R_b V_F}{R_a R_b + R_a R_c + R_b R_c} - \frac{V_R + V_L + V_F}{3}$$

or

$$V_T' - V_T = \frac{R_b R_c (V_R - V_T) + R_a R_c (V_L - V_T) + R_a R_b (V_F - V_T)}{R_a R_b + R_a R_c + R_b R_c}$$

This last equation gives the difference in potential between the central terminal when the resistances are unequal and the central terminal when the resistances are equal in terms of the unequal resistances and the open circuit potentials of the limb electrodes with respect to their mean potential.

When R_b and R_c are equal, but R_a has a different value, we have

$$V_T' - V_T = \frac{R_b(V_R - V_T) + R_a(V_L - V_T) + R_a(V_F - V_T)}{2R_a + R_b}$$

and since $(V_R - V_T) = -(V_L - V_T) - (V_F - V_T)$, this gives

$$V_T' - V_T = \frac{(R_b - R_a)\ (V_R - V_T)}{2R_a + R_b}$$

REFERENCES

1. Wilson, F. N., Johnston, F. D., Macleod, A. G., and Barker, P. S.: Electrocardiograms That Represent the Potential Variations of a Single Electrode, Am. Heart J. **9**:447, 1934.
2. Goldberger, E.: A Simple, Indifferent, Electrocardiographic Electrode of Zero Potential and a Technique of Obtaining Augmented, Unipolar, Extremity Leads, Am. Heart J. **23**:483, 1942.
3. Einthoven, W., and Bijtel, J.: Ueber Stromleitung durch den Menschlichen Körper, Arch. f. d. ges. Physiol. **198**:439, 1923.
4. Einthoven, W., Bergansius, F. L., and Bijtel, J.: Die gleichzeitige Registrierung Elektrischen Erscheinungen Mittels zwei oder mehr Galvanomer und ihre Anwendung auf die Elektrokardiographie, Arch. f. d. ges. Physiol. **164**:167, 1916.
5. (a) Wilson, F. N., Macleod, A. G., and Barker, P. S.: The Accuracy of Einthoven's Equation, Am. Heart J. **7**:203, 1931.
   (b) Wilson, F. N., Macleod, A. G., and Barker, P. S.: The Potential Variations at the Apices of Einthoven's Triangle, Am. Heart J. **7**:207, 1931.
6. Helmholtz, H.: Ueber einige Gesetze der Verthelung elektrischer Strome im Körperlichen Leitern mit Anwendung auf die thierisch elektrische Versuche, Ann. d. Physik. J. Chem. Ser. 2 **89**:211, 1853.
7. Bryant, J. M., and Johnston, F. D.: Errors Encountered in the Use of the Goldberger Central Terminal, J. Soc. Clin. Investigation **25**:919, 1946.

NEUTRALIZATION OF THE ANTICOAGULANT EFFECTS OF HEPARIN WITH PROTAMINE (SALMINE)*

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THE anticoagulants, heparin and Dicumarol, are of proved value in the prevention and treatment of intravascular thrombosis. Their advantages and disadvantages have been clearly defined by Allen.[1] One disadvantage common to both is that they may cause bleeding. Bleeding as the result of a Dicumarol-induced prothrombin deficiency may be controlled by the intravenous injection of large doses of vitamin K. Hemorrhage due to a prolonged coagulation time resulting from administration of heparin may be controlled only by discontinuing the administration of heparin or by blood transfusion. These procedures may not prevent the hemorrhage from reaching serious proportions.

Protamines are known to neutralize the effects of heparin both in vitro and in vivo. Protamines appear to have certain toxic effects[2-7] when administered in varying doses to different species of animals. The assumption appears in the literature that because of their toxicity the protamines cannot be safely administered to human subjects. Jorpes and associates,[8] however, said that certain doses of some protamines can be administered to human beings to neutralize the effects of heparin without producing toxic effects. Lam and Cowley[9] have recently stated that protamines may be used to neutralize the effects of heparin on human subjects.

Chargaff and Olson,[3] in 1937, discovered that the anticoagulant effect of heparin in animals was entirely stopped by the intravenous injection of a protamine. They suggested that this method of treatment might be used clinically to interrupt the anticoagulant action of heparin at any time. Jaques, Charles, and Best[4] confirmed the observations of Chargaff and Olson[3] and found that a certain amount of salmine was required to neutralize the effect of a given amount of heparin. Jorpes and co-workers,[8] working in Sweden in 1939, injected a protamine intravenously into human subjects. No undesirable reactions were observed after the intravenous administration of 20 to 75 mg. of a 2 per cent solution of clupeine sulfate to healthy persons, and the anticoagulant effect of heparin was abolished either partially or completely.

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Thompson,[2] in 1900, was the first to show that protamines produced toxic reactions in animals. He found that the intravenous administration of a protamine produced a fall in the arterial blood pressure of dogs. Chargaff and Olson[3] and Jaques, Charles, and Best[4] have shown that protamines are toxic when injected intravenously into dogs. Vartiainen and Marble[5] found that the minimal lethal dose of salmine for rabbits and mice was 200 to 300 mg. per kilogram of body weight when the protamine was administered subcutaneously. Shelley, Hodgkins, and Visscher[6] found that salmine sulfate produced death when administered intravenously to guinea pigs in doses of 6.0 to 12 mg. per 100 grams of body weight. Typical anaphylactoid symptoms occurred before the animals died. Shelley and Tarail[7] injected lethal doses of salmine sulfate into the portal veins of rats and guinea pigs and found that the protamine produced hepatic vascular occlusion.

A search of the literature has disclosed only one article[8] that contains data regarding the intravenous administration of protamines to human subjects. The literature, however, does contain conflicting opinions regarding the administration of protamines to man.

Mason[10] said that protamines are toxic if administered in any form intravenously. Lindgren and Wilander,[11] Leissner,[12] and Ravdin[13] advised the use of protamines for neutralization of heparin in man; however, they provided no data in their reports. Ferguson,[14] in 1946, suggested that toxic reactions caused by overdoses of heparin should be treated with protamine zinc insulin.

EXPERIMENTAL INVESTIGATION

Neutralization of Heparin in Vitro.—We found by in vitro studies that 1.5 mg. of salmine sulfate* neutralized 1.0 mg. of heparin.* A similar ratio was found to exist for 0.5 mg. of heparin because 0.8 mg. of salmine sulfate was required to neutralize this amount of heparin. Protamines exert an anticoagulant effect in vitro. When salmine is present in exactly the amount needed to neutralize heparin, the coagulation time is normal. When heparin or salmine is present in excess in vitro, the coagulation time is prolonged.

Toxicity.—Studies on animals, a complete report of which will be published later, showed that the lethal dose of salmine sulfate when injected intravenously into guinea pigs was 6.0 mg. per 100 grams of body weight. In unanesthetized rabbits, salmine sulfate was injected intravenously in doses as high as 90 mg. per kilogram of body weight without producing severe toxic reactions. In the anesthetized rabbit, salmine sulfate injected intravenously in doses of 10 mg. per kilogram of body weight produced a rapid, transient, moderate fall in arterial blood pressure (Fig. 1,*a*). Intravenous administration of 60 mg. of salmine sulfate per kilogram of body weight to anesthetized rabbits produced death within a short time (Fig. 1,*b*).

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*The heparin used in this study was obtained through the courtesy of the Abbott Laboratories, North Chicago, Ill. The salmine sulfate was obtained through the courtesy of Eli Lilly & Company, Indianapolis, Ind.

Intravenous injection of 1.5 to 2.0 mg. of salmine sulfate per kilogram of body weight into unanesthetized dogs did not produce any toxic effects. Similar injection of 2.0 mg. of salmine sulfate per kilogram of body weight into anesthetized dogs produced a marked transient fall in arterial blood pressure.

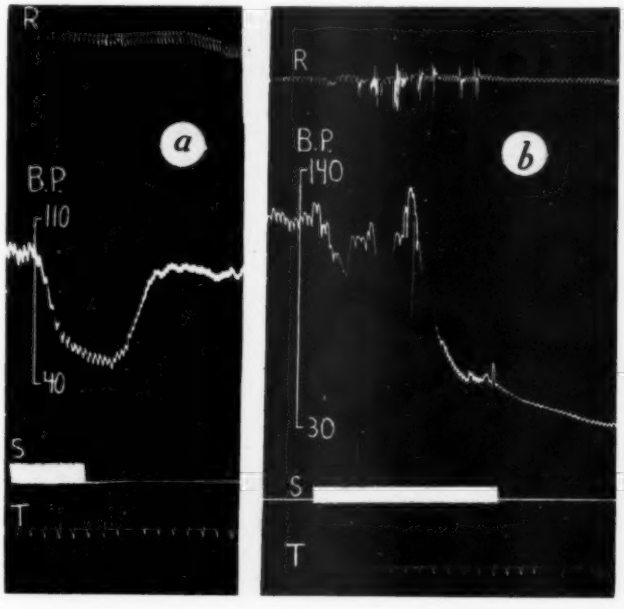

Fig. 1.—*a*, Effect of intravenous injection (at Signal S) of 10 mg. of salmine sulfate per kilogram of body weight on the blood pressure (*B.P.*) and respiration (*R*) of an anesthetized rabbit. (*T* represents the time in intervals of five seconds.)

b, Effect of intravenous injection of 60 mg. of salmine sulfate per kilogram of body weight on the blood pressure of an anesthetized rabbit.

Neutralization of Heparin in Vivo.—After the coagulation time of the blood of three dogs had been determined, 1.0 mg. of heparin per kilogram of body weight was injected intravenously into each animal. The coagulation time of the blood of each animal then was determined at intervals of fifteen minutes until it returned to normal. The intravenous injection of 1.0 mg. of heparin per kilogram of body weight prolonged the coagulation time beyond forty minutes within fifteen minutes after the injection. It was still elevated thirty minutes later but returned to normal within one hour (Fig. 2,*a*). With this to serve as a control, a second series of four dogs received intravenous injections of 1.0 mg. of heparin per kilogram of body weight after the normal coagulation time was determined. Fifteen minutes later, blood was withdrawn for determination of the coagulation time and 1.5 mg. of salmine sulfate per kilogram of body weight was injected intravenously through the same needle. The coagulation time was determined five minutes after the salmine sulfate was injected and at intervals of thirty, forty-five, and sixty minutes after the heparin was injected. In this series of four dogs, the clotting time was elevated beyond fifty minutes, fifteen minutes

after the injection of heparin. After the injection of salmine sulfate, the clotting time rapidly returned to normal within five minutes (Fig. 2,*b*). No toxic reactions were noted in these animals.

In another series of experiments, heparin sodium in Pitkin's menstruum* was administered intramuscularly in doses of 12 mg. per kilogram of body weight to four dogs. The coagulation time was determined at varying intervals for

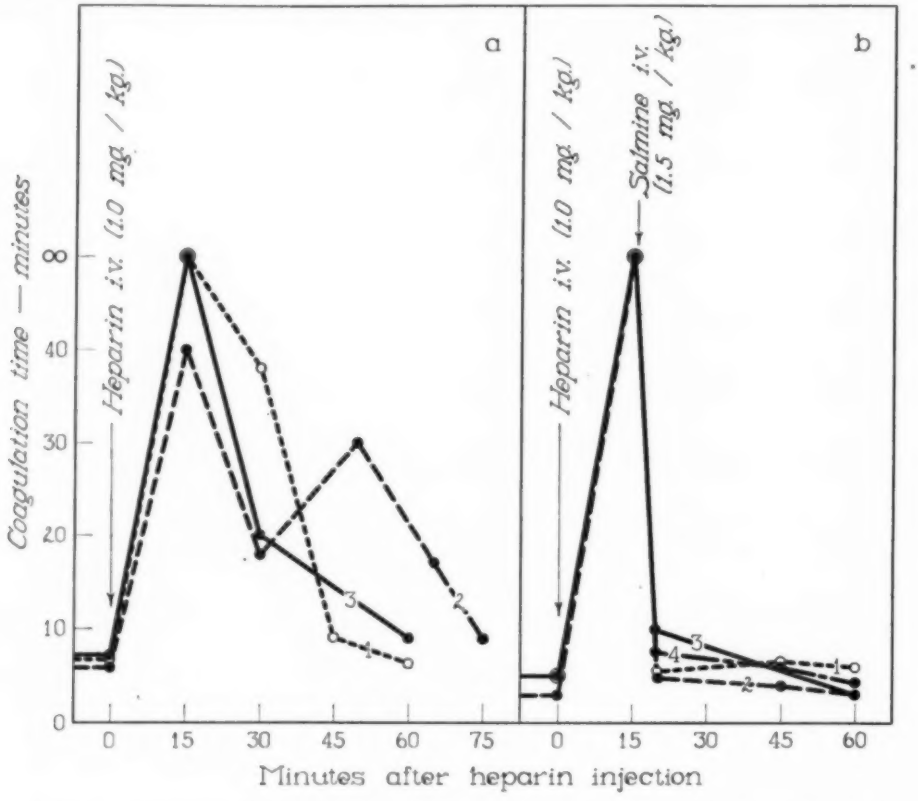

Fig. 2.—*a*, Effect of a single intravenous injection of 1.0 mg. of heparin per kilogram of body weight on the coagulation time of the blood of three dogs.

***b*, Effect of a single intravenous injection of 1.5 mg. of salmine sulfate per kilogram of body weight on the anticoagulant effect produced by the intravenous administration of 1.0 mg. of heparin per kilogram to each of four dogs.**

twenty-four hours after the heparin was administered. The coagulation time was more than fifty minutes for from nine to twelve hours after the injection, but it then gradually returned to normal (Fig. 3,*a*). These results were used as a control. A similar dose of heparin in Pitkin's menstruum then was administered intramuscularly to one dog. The coagulation time was determined two hours after the heparin was administered. One milligram of salmine sulfate per kilogram of body weight was administered intravenously immediately after the

*The Pitkin menstruum was obtained through the courtesy of the Abbott Laboratories. Each cubic centimeter of this menstruum contained 100 mg. of sodium heparin, 180 mg. of gelatin, 80 mg. of dextrose, and 0.01 c.c. of glacial acetic acid in distilled water.

specimen of blood had been withdrawn for the determination of the coagulation time, and a similar dose of salmine was administered intravenously fifteen minutes later. The coagulation time was determined at various intervals for twenty-four hours. The injections of salmine sulfate caused the coagulation time to return nearly to normal for forty-five minutes, but it then became prolonged (Fig. 3,*b*).

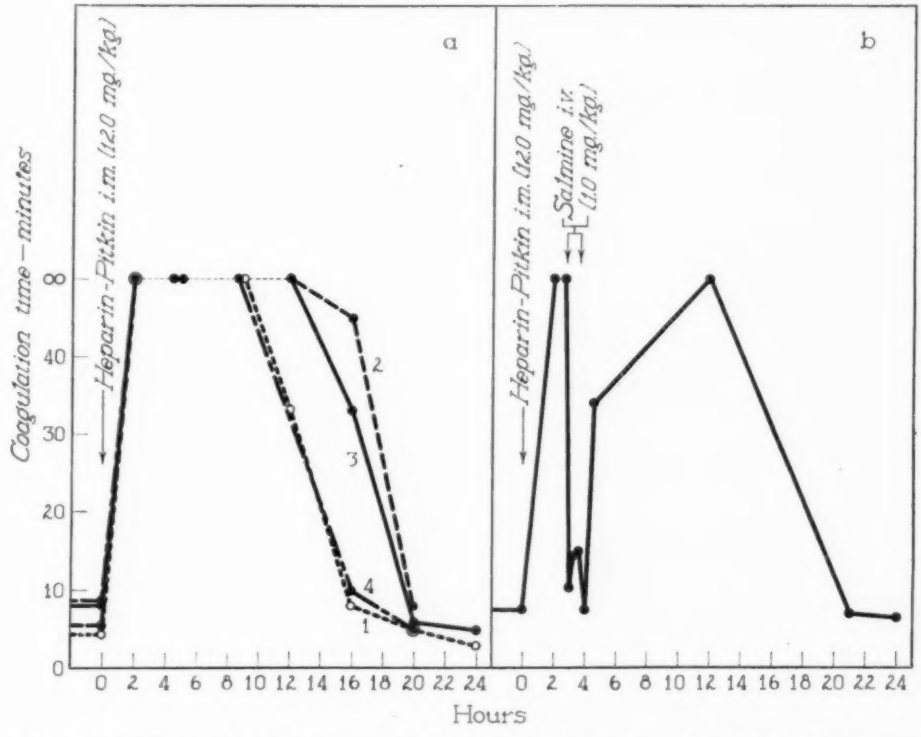

Fig. 3.—*a*, Effect of a single intramuscular injection of 12 mg. of heparin (in Pitkin's menstruum) per kilogram of body weight on the coagulation time of the blood of four dogs.

***b*, The effect of two intravenous injections of salmine sulfate (each dose 1.0 mg. per kilogram of body weight), given fifteen minutes apart, on the anticoagulant effect produced by the intramuscular administration of one dose of 12 mg. of heparin (in Pitkin's menstruum) per kilogram of body weight to a dog.**

CLINICAL OBSERVATIONS

Ten persons kindly consented to undergo certain harmless tests in order that we might determine the amount of salmine sulfate required to neutralize the effects produced by a specific amount of heparin.

Attempts were made to standardize several factors known to influence the coagulation of blood. All equipment was cleansed thoroughly each time it was used. Needles were kept sharp. Trauma upon entering the vein was kept at a minimum. All coagulation times were determined by the Lee-White method. One milliliter of venous blood was placed in a test tube of 8.0 mm. bore that had been rinsed with physiologic salt solution. The tube was tilted at intervals of

thirty seconds until blood no longer flowed in it. All test tubes were kept in an aluminum rack which was placed in a water bath (37°C.) with thermostat temperature control.

For purposes of control, we determined the anticoagulant effect produced by the intravenous administration of 50 mg. of heparin. The coagulation time of the blood of four of the ten persons was determined before the injection, and fifteen, forty-five, and sixty minutes after the injection of heparin. The average normal coagulation time was four minutes and fifteen seconds. At fifteen minutes after the injection of heparin, the average coagulation time was eighteen minutes and fifty-five seconds, at forty-five minutes it was seventeen minutes and twenty-two seconds, and at sixty minutes it was seventeen minutes and sixty-five seconds.

The average coagulation time of the blood of five other persons was determined before 50 mg. of heparin was administered intravenously and at intervals of one, two, and three hours after the heparin was administered. The average normal coagulation time of the blood of these five persons was four minutes and eighteen seconds. At one hour after injection of the heparin the average coagulation time was seventeen minutes and twenty seconds, at two hours it was ten minutes and four seconds, and at three hours it was five minutes and thirty-two seconds. The intravenous administration of 50 mg. of heparin increased the coagulation time to about four times normal for one hour. The coagulation time then decreased gradually and became normal within three hours.

The following plan was used in all cases in which salmine sulfate was administered. After the normal coagulation time was determined, 50 mg. of heparin was administered intravenously. The coagulation time then was determined at intervals of fifteen, thirty, forty-five, sixty, 120, and 180 minutes. Fifteen minutes after the heparin was administered, salmine sulfate was injected intravenously through the same needle that was used to withdraw blood for determination of the coagulation time. Since a period of ten minutes was required for the injection of the salmine sulfate, the blood that was withdrawn for determination of the coagulation time thirty minutes after the administration of heparin actually was withdrawn only five minutes after the completion of the injection of the salmine sulfate.

Neutralization of 50 mg. of Heparin in Man.—A series of ten persons received 50 mg. of heparin intravenously. Fifteen minutes after the injection of heparin, salmine sulfate was administered intravenously to all of the ten persons in doses ranging from 15 to 50 milligrams. When administered in doses of 15 and 25 mg., salmine sulfate was not effective in returning the coagulation time to normal. In cases in which 40 to 50 mg. of salmine sulfate was administered, the coagulation time returned to its normal level within five minutes after the injection of the salmine sulfate and remained there for three hours, during which the coagulation time was determined (Figs. 4 and 5).

No toxic manifestations were noted during or after the administration of salmine sulfate to the human subjects used in the study. No subjective or objective changes appeared. There were no changes in blood pressure, pulse rate, or respiratory rate.

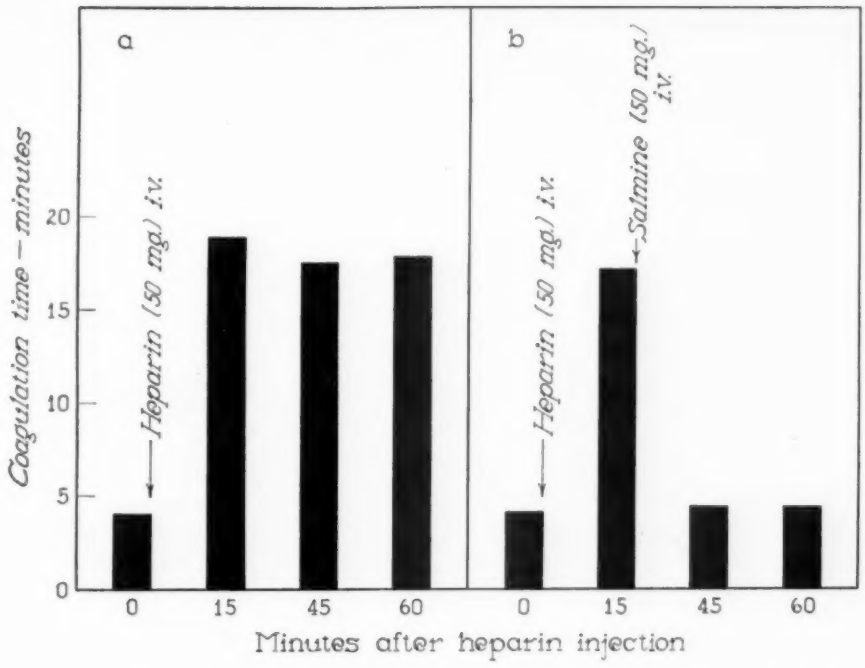

Fig. 4.—*a*, Average effect of a single intravenous injection of 50 mg. of heparin on the coagulation time of the blood of four persons. Coagulation time determined at intervals of fifteen minutes for one hour.

b, Average effect of a single intravenous injection of 50 mg. of salmine sulfate on the anticoagulant effect produced by the intravenous administration of 50 mg. of heparin to four persons. The salmine was injected fifteen minutes after the injection of heparin. Coagulation times were determined at intervals of fifteen minutes for one hour.

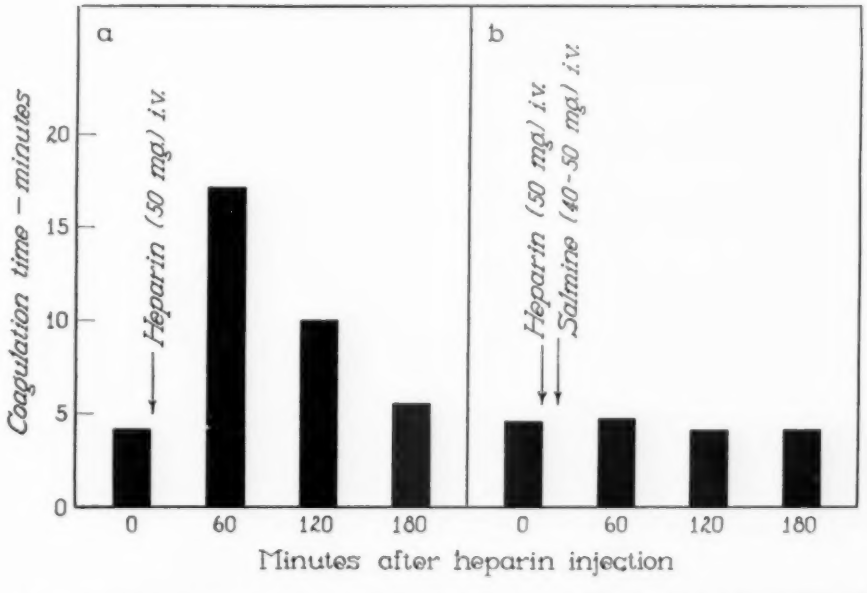

Fig. 5.—*a*, Average effect of a single intravenous injection of 50 mg. of heparin on the coagulation time of the blood of five persons. Coagulation time determined at intervals of one hour for three hours.

b, Average effect of intravenous injection of 40 to 50 mg. of salmine sulfate on the anticoagulant effect produced by the intravenous injection of 50 mg. of heparin to five persons. The salmine sulfate was injected fifteen minutes after the injection of heparin. Coagulation times were determined at intervals of one hour for three hours.

COMMENT

A quantitative relationship was found to exist between salmine sulfate and heparin when titration studies were made in vitro. One and one-half milligrams of salmine sulfate was required to neutralize 1.0 mg. of heparin. This ratio is not the same as that reported by Jaques and his co-workers[4]; however, they used different preparations of heparin and protamine. Varying ratios probably will be obtained when different preparations are used. In addition, the type of blood used for the titration studies should be considered when comparisons are made. Dog blood was used in our in vitro experiments.

The ratio between the amount of salmine sulfate required to neutralize a definite amount of heparin in man appeared to be about 1:1 when fifteen minutes had elapsed between the injection of heparin and the injection of salmine sulfate. If more time would elapse after the injection of heparin, proportionately less heparin would be present in the blood and, consequently, less salmine sulfate should be needed for neutralization.

The thrombocytes, leucocytes, fibrinogen, and prothrombin were not studied during our observations. Chargaff and Olson[3] stated that the hematocrit reading, the thrombocyte count, the concentration of hemoglobin, and the erythrocyte count were not altered in dogs after the intravenous injection of protamine. Thompson[2] stated that there was a decrease in the number of leucocytes in the dogs he studied after intravenous injection of protamines. Mylon, Winternitz, and De Sütö-Nagy[15] reported that protamine precipitates fibrinogen.

It is the consensus of authors[16-19] that protamines are nonantigenic. The report of Walther and Ammon[20] is in disagreement with this view. However, the shock dose they used was so large that a toxic reaction to histamine, independent of an antibody-antigen reaction, may have been the cause of death.

Fifty milligrams of heparin injected intravenously every four hours is the standard dose used in most parts of this country in the prevention and treatment of vascular thromboembolic emergencies. Consequently, no attempt was made to neutralize larger doses of heparin injected by the intermittent intravenous method.

It was observed, however, that salmine sulfate temporarily neutralized heparin which had been incorporated in Pitkin's menstruum and injected intramuscularly into dogs. The neutralizing effect of one intravenous injection of salmine sulfate was of short duration; that is, it lasted about fifteen minutes. Two intravenous injections of salmine sulfate, given fifteen minutes apart, caused the coagulation time to return rapidly to normal and to remain at a normal level for forty-five minutes (Fig. 3,*a* and *b*). In view of these findings, it seems likely that repeated or continuous intravenous injections of small doses of salmine sulfate may be used as an effective means of controlling the effects of heparin which has been incorporated in a delaying menstruum and administered subcutaneously or intramuscularly to human subjects.

Several theoretical problems deserve some consideration in a study of this kind. Does the possibility exist that a sudden reduction of an elevated blood

coagulation time to normal initiates vascular thrombosis? In the present study no clinical evidence of thrombosis was observed after the intravenous injection of salmine sulfate. Another consideration is whether the blood will become hypercoagulable when more salmine sulfate is injected intravenously than is required for neutralization of heparin. It has been demonstrated by Jaques[21] and also in this study that there is a quantitative neutralization of heparin and that if an excess of salmine sulfate exists in the blood in vitro an anticoagulant effect is produced. In vivo, no anticoagulant effect due to protamines was observed with doses which produced no toxic manifestations. In vitro, protamines do exert an anticoagulant effect on whole blood. Chargaff[22,23] explained the anticoagulant effect of protamines on the basis that they combine with and inhibit the clotting activator, cephalin. Ferguson[24] expressed the opinion that salmine was antiprothrombic in the first phase and fibrinoplastic in the second phase of blood clotting. Mylon and his co-workers[15] said that prolongation of the blood clotting time undoubtedly resulted from the partial precipitation of fibrinogen. Tocantins[25] has shown that plasma to which an appropriate amount of protamine has been added will show a prolongation of the plasma clotting time and the appearance of a degree of antithromboplastic activity closely resembling that observed in hemophilic plasma. No abnormal acceleration of coagulation time of whole blood in vivo was observed during this study.

It was observed that the speed of injection of salmine sulfate is an important factor in producing toxic reactions in animals. The more slowly it was administered, the less frequent were the toxic reactions. For this reason, ten minutes were allowed for the injection of salmine into man. Although this is an arbitrary time limit, the slow intravenous injection of salmine into man is to be recommended.

Since the risk of hemorrhage from the intermittent intravenous injection of heparin is minimal, the need for protamines will not be great. In a few cases, particularly those in which operation is performed and prompt neutralization of heparin is desired, this protamine should be of value. With the subcutaneous and intramuscular administration of heparin in delaying menstruums and with new developments in the field of vascular surgery, a need for rapid and effective control of heparin becomes apparent.

SUMMARY AND CONCLUSIONS

The protamine, salmine, was found to have toxic effects when it was administered intravenously in large doses to guinea pigs, rabbits, and dogs. When small doses, such as 1.0 mg. per kilogram, were administered, toxic effects were not noted.

Salmine neutralized the anticoagulant effect of intravenous injections of heparin into dogs. When heparin in Pitkin's menstruum was injected intramuscularly into dogs, the elevated coagulation time returned to normal temporarily after the intravenous injection of salmine.

In man, the intravenous injection of 40 to 50 mg. of salmine sulfate neutralized promptly the anticoagulant effect of 50 mg. of heparin, and when salmine sulfate was administered slowly in these doses it did not produce any reactions.

ACKNOWLEDGMENT

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REFERENCES

1. Allen, E. V.: The Clinical Use of Anticoagulants: Report of Treatment With Dicumarol in 1,686 Postoperative Cases, J. A. M. A. **134**:323, 1947.
2. Thompson, W. H.: Die physiologische Wirkung der Protamine und ihrer Spaltungsprodukte, Hoppe-Seyler's Ztschr. f. physiol. Chem. **29**:1, 1900.
3. Chargaff, Erwin, and Olson, K. B.: Studies on the Chemistry of Blood Coagulation. VI. Studies on the Action of Heparin and Other Anticoagulants. The Influence of Protamine on the Anticoagulant Effect In Vivo, J. Biol. Chem. **122**:153, 1937-1938.
4. Jaques, L. B., Charles, A. F., and Best, C. H.: The Administration of Heparin, Acta med. Scandinav. (Suppl.) **90**:190, 1938.
5. Vartiainen, Ilmari, and Marble, Alexander: The Effect of Subcutaneous Administration of Protamine (Salmine) to Rabbits and Mice, J. Lab. & Clin. Med. **26**:1416, 1941.
6. Shelley, W. B., Hodgkins, Myrtle P., and Visscher, M. B.: Studies on the Toxicity of Protamine, Proc. Soc. Exper. Biol. & Med. **50**:300, 1942.
7. Shelley, W. B., and Tarail, R.: Hepatic Vascular Occlusion Following Lethal Doses of Salmine Sulfate, Proc. Soc. Exper. Biol. & Med. **52**:215, 1943.
8. Jorpes, E., Edman, P., and Thanning, T.: Neutralisation of Action of Heparin by Protamine, Lancet **2**:975, 1939.
9. Lam, C. R., and Cowley, L. L.: Personal communication to the authors.
10. Mason, M. F.: Heparin: A Review of Its History, Chemistry, Physiology and Clinical Applications, Surgery **5**:621, 1939.
11. Lindgren, Stig, and Wilander, Olaf: The Use of Heparin in Vascular Surgery, Acta med. Scandinav. **107**:148, 1941.
12. Leissner, Herman: The Use of Heparin in Obstetric Practice as a Means of Preventing Thrombosis, Acta med. Scandinav. **107**:127, 1941.
13. Ravdin, I. S.: Heparin, Am. J. M. Sc. **201**:299, 1941.
14. Ferguson, J. H.: Blood Coagulation, Thrombosis, and Hemorrhagic Disorders, Ann. Rev. Physiol. **8**:231, 1946.
15. Mylon, E., Winternitz, M. C., and de Sütö-Nagy, G. J.: The Determination of Fibrinogen With Protamine, J. Biol. Chem. **143**:21, 1942.
16. Taylor, A. E.: Chemical Studies in Cytolysis, J. Biol. Chem. **5**:311, 1908.
17. Wells, H. G.: The Chemical Aspects of Immunity, New York, 1929, Chemical Catalog Company, p. 28.
18. Kern, R. A., and Langner, P. H.: Protamine and Allergy. I. Nature of the Local Reactions After Injections of Protamine Zinc Insulin. II. Induction of Sensitivity to Insulin by Injections of Protamine Zinc Insulin, J. A. M. A. **113**:198, 1939.
19. Gutman, N.: Recherches sur le caractère antigénique de la clupéine couplée a des noyaux aromatiques, Rev. d'immunol. **4**:111, 1938.
20. Walther G., and Ammon, R.: Anaphylaktischer Schock nach Protamin, Klin. Wchnschr. **18**:288, 1939.
21. Jaques, L. B.: The Reaction of Heparin With Proteins and Complex Bases, Biochem. J. **37**:189, 1943.
22. Chargaff, Erwin: Studies on the Chemistry of Blood Coagulation. VII. Protamines and Blood Clotting, J. Biol. Chem. **125**:671, 1938.
23. Chargaff, Erwin, and Ziff, Morris: The Compounds Between Phosphatides and Basic Proteins, J. Biol. Chem. **131**:25, 1939.
24. Ferguson, J. H.: The Action of Heparin, Serum Albumin (Crystalline), and Salmine on Blood-Clotting Mechanisms (In Vitro), Am. J. Physiol. **130**:759, 1940.
25. Tocantins, L. M.: Cephalin, Protamine and Antithromboplastic Activity of Normal and Hemophilic Plasmas, Proc. Soc. Exper. Biol. & Med. **54**:94, 1943.

A COMPARISON OF PRECORDIAL ELECTROCARDIOGRAMS OBTAINED WITH CR, CL, CF, AND V LEADS

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CHICAGO, ILL.

PRECORDIAL leads in which the indifferent electrode is placed on one of the extremities do not record the true electrical changes occurring at the precordium, but are subject to distortions resulting from the potential variations of the indifferent electrode. The nature and magnitude of the distortion will vary, depending, among other things, on the anatomic position of the heart in the thorax. Although this has been recognized for some time, it has been assumed by many that these distortions are small in magnitude and do not influence the interpretation of the precordial electrocardiogram. Among the several attempts to obtain a true unipolar lead, one which is free from such distortion, the central terminal method of Wilson[1] has received the widest attention in clinical electrocardiography. It can be shown mathematically that the potential of the central terminal is equal to zero, provided that (a) the heart is considered electrically equivalent to a small dipole, (b) the body is considered a large homogeneous volume conductor, (c) the extremities are considered to form the apices of an equilateral triangle in the center of which the heart is located, and (d) the heart and extremities are considered to lie in the same plane.[1,2] Considerable difference of opinion exists as to the accuracy of these assumptions. Actual measurement of the potential of the central terminal has shown it to be not greater than 0.3 to 0.36 mv.,[3,4,5,6] that is, 3.0 to 3.5 mm., in tracings as ordinarily standardized.

Several studies have been made comparing precordial leads obtained with the indifferent electrode on the right arm, left arm, left leg, and, in some studies, with the chest electrode connected to the central terminal.[7,8,9a,9b,9c,10,11,12] The results of these studies have been uniform in demonstrating that differences between CR, CL, CF, and V leads do exist, but the conclusions derived have been divergent. Groedel,[9a] Wolferth and Wood,[13] and Alzamora Castro[12] stated that the type of precordial lead used could influence the interpretation of the electrocardiogram, whereas Hayos and Tomayo[10] concluded that the observed differences were essentially unimportant. In a previous communication from this laboratory, the latter view was upheld.[8] The results of the present study necessitate some revision of the conclusions stated in the previous paper. It is

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the purpose of this report to describe the differences among CR, CL, CF, and V leads taken at identical precordial positions and to cite four types of electrocardiograms we have observed in which these differences may influence the interpretation of the electrocardiogram.

MATERIAL AND METHOD

Standard limb, precordial, and aV extremity leads (taken by the Goldberger method,[14] but with the 5,000 ohm resistances retained) were taken on a group of forty-four normal adults of varying ages. The seven precordial positions were used, and at each one, without the chest electrode being moved, the indifferent electrode was attached in turn to the right arm, left arm, left leg, and the central terminal by means of a lead selector switch. Similar electrocardiograms were taken on patients with posterior wall infarction and pulmonary emphysema and on others who showed electrocardiographic abnormalities thought to be partly due to the effect of the potential of the indifferent electrode.

The amplitudes of the various deflections in the normal group were measured and tabulated according to the direction of the QRS axis. The mean and range were determined for each precordial position and for the aV leads. The values for the QRS and T deflections in the V extremity leads (obtained by multiplication of the deflections in the aV leads by two-thirds) were subtracted algebraically from the corresponding deflection in the V precordial lead to obtain the predicted CR, CL, and CF lead at the given position. The values so obtained were compared with the observed values in the CR, CL, and CF leads and the differences noted.

RESULTS

1. The minimum, maximum, and mean deflection of P, R, S, and T as observed in the different types of precordial leads are listed in Tables 1,*A*, 1,*B*, and 1,*C*. The P and T deflections were tallest in CR leads and smallest in CF leads at all precordial positions for all directions of the QRS axis. The R wave was tallest in CR leads and smallest in CF leads when the QRS axis was plus 35° to plus 90°, and smallest in CL leads when the QRS axis was 0° to plus 34°. The S wave was largest in CL leads when the direction of the QRS axis was to the left of plus 35° and largest in CF leads when the QRS axis was to the right of plus 35°. All the deflections in V leads tended to resemble CL leads when the direction of the QRS axis was to the right of 35°. The R and S deflections tended to resemble those in CF leads when the direction of the QRS axis was to the left of plus 35°. However, the P and T deflections in V leads resembled those in CL leads rather than in CF leads as would be expected. The explanation for this is not entirely clear. No significant differences were observed in regard to Q waves or S-T deviations.

TABLE 1,*A*. THE AMPLITUDE OF THE DEFLECTIONS IN VARIOUS PRECORDIAL LEADS (QRS AXIS 0 TO +34°; TEN SUBJECTS)

DEFLECTION	PRECORDIAL POSITION	CR			CF			CL			V		
		MIN. (MM.)	MEAN (MM.)	MAX. (MM.)	MIN. (MM.)	MEAN (MM.)	MAX. (MM.)	MIN. (MM.)	MEAN (MM.)	MAX. (MM.)	MIN. (MM.)	MEAN (MM.)	MAX. (MM.)
P	1	0.3	0.9	1.6	−1.1	−0.4	0.8	0.8	0.4	1.5	0	0.4	1.2
	2	−1.1	0.9	2.0	−0.8	0.1	0.8	0.3	0.7	1.4	0.1	0.6	1.4
	3	0.4	1.0	1.9	−0.5	−0.2	0.3	0.1	0.5	0.9	0.1	0.4	0.8
	4	0.8	1.0	1.7	−0.3	0.1	0.6	0.2	0.5	1.1	0.2	0.4	0.9
	5	0.7	1.0	1.4	−0.2	0.1	0.2	0.1	0.4	1.1	0.2	0.4	0.6
	6	0.6	1.1	1.8	−0.2	0.1	0.2	0	0.3	0.9	0.2	0.3	0.5
	7	0.5	0.9	1.2	−0.3	0	0.3	0	0.3	1.0	0.2	0.4	0.5
R	1	0.6	3.3	7.8	0	1.8	4.2	0.6	2.3	4.1	0.2	2.3	4.7
	2	2.4	7.9	13.9	1.0	5.1	8.9	1.6	4.5	7.1	1.6	5.6	9.4
	3	4.7	14.3	23.9	2.4	7.6	17.9	4.1	7.5	13.5	3.1	9.8	18.8
	4	9.1	19.3	27.8	3.2	12.0	20.9	2.9	11.0	19.1	5.8	13.9	22.0
	5	13.8	20.4	28.0	8.8	13.8	25.2	4.8	11.7	24.8	10.4	15.7	28.4
	6	11.5	16.9	29.8	6.1	10.3	22.5	5.2	9.2	18.0	7.1	12.1	23.8
	7	10.8	15.0	20.7	4.5	7.7	13.5	3.5	6.7	9.8	6.6	9.2	14.0
S	1	0.3	5.9	10.6	3.5	10.7	15.9	4.9	12.5	18.3	3.2	9.3	13.1
	2	2.5	9.3	18.8	3.3	12.2	25.5	4.8	13.2	26.2	3.8	11.4	24.1
	3	0	6.0	15.8	0.8	7.0	16.5	2.0	8.4	17.1	1.3	7.0	16.9
	4	0	3.3	9.8	0	3.7	8.7	0	3.0	11.4	0	3.5	7.8
	5	0	0.6	1.9	0	0.5	1.5	0	0.8	2.2	0	0.6	1.7
	6	0	0.2	0.9	0	0.1	0.9	0	0.4	1.7	0	0.2	1.0
	7	0	0	0.2	0	0	0	0	0.3	1.9	0	0	0
T	1	0.3	1.5	3.2	−3.2	−1.0	1.4	−2.9	−0.9	1.2	−2.2	0.3	1.8
	2	2.9	5.2	9.9	−0.5	3.2	7.0	1.2	3.4	5.7	0.6	3.9	7.5
	3	3.9	6.3	9.9	2.5	4.2	5.9	2.8	4.3	6.2	3.2	4.8	7.0
	4	2.9	5.3	10.2	2.1	3.9	6.0	1.4	4.2	7.5	2.8	4.6	7.9
	5	1.7	5.0	8.1	0.8	2.7	4.9	0.6	3.2	5.9	1.4	3.6	6.4
	6	0.8	4.1	7.9	0.4	1.8	3.8	0.2	2.3	4.7	0.8	2.8	4.9
	7	1.1	3.6	6.5	0	1.2	2.7	1.1	1.6	3.3	0.8	2.2	3.9

TABLE 1,*B*. THE AMPLITUDE OF THE DEFLECTIONS IN VARIOUS PRECORDIAL LEADS (QRS AXIS +35° TO +59°; TWELVE SUBJECTS)

DEFLECTION	PRECORDIAL POSITION	CR			CF			CL			V		
		MIN. (MM.)	MEAN (MM.)	MAX. (MM.)	MIN. (MM.)	MEAN (MM.)	MAX. (MM.)	MIN. (MM.)	MEAN (MM.)	MAX. (MM.)	MIN. (MM.)	MEAN (MM.)	MAX. (MM.)
P	1	0.5	1.0	2.0	−1.5	0	0.3	−0.2	0.4	1.1	0	0.6	3.0
	2	0.5	0.9	1.4	−1.0	0.1	0.4	0	0.5	0.9	0.3	0.5	0.9
	3	0.2	0.9	1.4	−0.5	0.1	0.9	0.2	0.5	0.9	0.2	0.4	0.8
	4	0.3	1.0	1.4	−0.2	0.1	0.4	0.2	0.5	0.9	0.1	0.4	0.7
	5	0.5	0.9	1.4	−0.2	0.2	0.3	0	0.3	0.8	0	0.4	0.7
	6	0.3	0.9	1.2	−0.2	0.1	0.3	0	0.4	0.7	0	0.3	0.6
	7	0.3	0.8	1.1	−0.5	0	0.4	0	0.3	0.9	0.2	0.3	0.5
R	1	1.3	4.7	6.4	1.2	3.2	4.9	1.1	3.5	6.7	1.4	3.7	5.2
	2	1.5	8.9	19.9	1.2	5.6	10.0	1.8	5.9	9.0	1.5	6.7	12.9
	3	2.1	14.4	27.2	1.1	7.2	16.7	1.5	8.8	12.6	1.7	10.1	18.9
	4	12.2	20.7	29.0	7.4	11.7	19.9	9.4	14.5	21.9	7.8	15.5	22.6
	5	15.9	19.4	26.8	3.8	10.9	20.2	8.9	13.5	21.2	10.8	14.6	19.9
	6	11.5	16.0	21.6	4.2	7.1	17.1	5.6	10.1	20.1	7.6	10.9	18.7
	7	9.1	13.1	16.7	0.3	4.6	12.2	3.0	7.6	15.1	5.7	8.2	13.8
S	1	2.9	8.4	14.6	9.8	14.4	21.9	3.8	12.1	18.8	5.2	11.4	18.7
	2	2.1	10.1	16.3	3.6	13.9	21.9	4.1	12.5	20.8	5.0	11.9	18.9
	3	0	5.5	11.4	0.9	6.9	13.9	0.7	6.0	9.8	0.5	6.2	10.8
	4	0	2.4	8.2	0	2.9	10.9	0	2.7	8.1	0	2.6	8.1
	5	0	0.9	3.1	0	1.3	5.7	0	0.9	1.5	0	0.9	3.3
	6	0	0.4	1.8	0	0.3	2.5	0	0.4	2.4	0	0.3	1.1
	7	0	0.3	1.6	0	0.1	1.4	0	0.1	0.8	0	0.1	0.6
T	1	1.1	3.1	6.6	−4.6	0	3.5	−1.1	1.2	4.2	−3.2	1.0	3.8
	2	3.0	5.5	11.9	−0.8	3.9	8.6	1.1	4.4	11.0	1.2	4.7	11.5
	3	2.9	6.2	12.0	1.5	3.9	8.9	2.0	4.3	9.7	2.2	3.9	10.2
	4	2.1	5.7	10.2	1.8	3.3	4.7	1.5	3.9	6.5	1.8	4.4	7.7
	5	2.0	5.0	11.1	0.9	2.3	4.8	0.8	3.1	7.3	1.2	3.5	7.5
	6	1.8	4.1	8.9	0.1	1.5	3.5	0.4	2.1	4.7	0.8	2.5	5.9
	7	0.8	3.4	7.1	−0.2	0.9	2.7	0	1.7	3.5	0.3	2.0	4.1

TABLE 1,*C*. THE AMPLITUDE OF THE DEFLECTIONS IN VARIOUS PRECORDIAL LEADS (QRS AXIS +60° TO +90°; TWENTY-TWO SUBJECTS)

DEFLECTION	PRECORDIAL POSITION	CR			CF			CL			V		
		MIN. (MM.)	MEAN (MM.)	MAX. (MM.)	MIN. (MM.)	MEAN (MM.)	MAX. (MM.)	MIN. (MM.)	MEAN (MM.)	MAX. (MM.)	MIN. (MM.)	MEAN (MM.)	MAX. (MM.)
P	1	−0.3	0.9	1.5	−1.5	−0.9	0.7	0	0.6	1.1	−0.4	0.5	1.0
	2	0.3	0.9	1.4	−1.5	−0.4	1.0	0.3	0.6	0.9	−0.3	0.7	0.9
	3	0.6	1.0	1.9	−1.0	0.2	0.5	0.2	0.6	1.5	0.2	0.5	1.1
	4	0.5	1.0	1.7	−0.5	−0.1	0.5	0.2	0.6	1.1	0.3	0.5	1.1
	5	0.6	1.1	1.8	−0.5	−0.1	0.3	0	0.6	1.4	0.1	0.5	1.1
	6	0.9	1.2	1.9	−0.6	−0.1	0.2	0.1	0.6	1.1	0.2	0.5	1.1
	7	0.7	1.1	1.7	−0.5	−0.1	0.2	0	0.6	1.2	0.2	0.6	1.3
R	1	0.8	4.0	9.7	0.8	2.2	7.7	1.1	3.1	6.9	1.5	3.3	6.9
	2	1.4	6.6	14.2	2.1	5.4	12.9	2.1	5.3	11.8	2.1	5.3	12.7
	3	5.4	10.9	28.0	2.2	6.6	17.3	3.0	8.5	24.7	4.1	8.7	23.5
	4	7.8	18.2	30.9	1.4	8.4	18.4	3.8	15.0	30.6	6.1	14.3	27.1
	5	4.9	17.7	29.5	0.8	6.2	13.3	7.8	14.3	27.1	5.8	12.9	21.8
	6	4.9	15.6	24.9	0.5	3.5	7.6	4.2	11.9	23.0	6.1	10.4	16.2
	7	3.1	13.1	19.5	0	1.9	5.2	3.9	10.2	18.6	4.2	8.6	15.7
S	1	3.3	9.7	18.4	3.8	18.9	28.8	1.7	10.9	25.8	2.2	12.7	25.9
	2	2.9	13.6	22.4	12.1	21.3	30.1	7.9	14.8	24.3	6.8	16.2	23.6
	3	0	9.3	19.8	0	13.4	29.2	0	8.7	19.1	0	10.2	21.1
	4	0	4.9	13.9	0	7.0	23.9	0	3.7	12.9	0	5.0	13.9
	5	0	1.4	4.4	0	2.1	7.9	0	0.7	3.9	0	1.1	5.1
	6	0	0.8	4.1	0	1.0	4.2	0	0.4	2.9	0	0.6	2.6
	7	0	0.6	2.7	0	0.8	3.1	0	0.2	1.8	0	0.3	1.4
T	1	−0.2	2.8	6.7	−2.4	−0.2	3.2	−1.9	1.7	5.7	−1.4	1.3	6.0
	2	0.2	6.5	11.9	−1.2	4.5	8.2	−0.6	5.4	10.1	−0.3	5.6	9.8
	3	0.8	7.3	12.9	−0.3	4.7	8.5	−0.3	5.7	10.8	−0.2	5.5	10.6
	4	2.2	6.6	10.9	0.2	3.6	7.9	0.2	4.7	9.0	1.4	5.0	9.1
	5	2.2	5.2	8.2	0	2.3	5.0	1.1	3.2	5.4	0.9	4.0	5.3
	6	1.8	4.1	5.8	−0.7	1.1	2.7	0.9	2.3	3.9	0.8	2.6	3.8
	7	1.4	3.4	5.5	−0.7	0.5	1.2	0.3	1.9	3.6	0.8	2.2	3.9

TABLE 2,A. THE PREDICTED AND OBSERVED VALUES FOR THE MEAN QRS DEFLECTIONS

	QRS AXIS 0° TO +34°							QRS AXIS +35° TO +59°							QRS AXIS +60° TO +90°						
	PRECORDIAL POSITION							PRECORDIAL POSITION							PRECORDIAL POSITION						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
V Observed	−7.0	−5.8	2.7	12.1	14.7	11.3	8.8	−13.5	−5.2	3.7	12.6	13.3	10.1	7.6	−9.4	−10.9	−1.6	9.2	11.5	9.3	7.8
V_R Observed				−7.5							−5.7							−5.1			
V_L Observed				2.5							0.7							−1.9			
V_F Observed				1.0							3.3							6.4			
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
CR Predicted	0.5	1.7	10.2	19.6	22.2	18.8	16.3	−7.8	0.5	9.4	18.3	19.0	15.8	13.3	−4.3	−5.8	3.5	14.3	16.6	14.4	12.9
Observed	−2.6	−1.4	8.2	15.3	17.9	16.0	14.4	−3.7	−1.2	8.8	17.6	17.9	14.9	12.1	−5.7	−7.0	1.5	13.1	15.7	14.1	11.8
Difference	3.1	3.1	2.0	4.3	4.3	2.8	1.9	4.1	1.7	0.6	0.7	1.1	0.9	1.2	1.4	1.2	2.0	1.2	0.9	0.3	1.1
CL Predicted	−9.5	−8.3	0.2	9.6	12.2	8.8	6.3	−14.2	−5.9	3.0	11.9	12.6	9.4	6.9	−7.5	−9.0	0.3	11.1	13.4	11.2	9.7
Observed	−10.2	−8.7	−1.0	7.8	10.6	7.1	6.1	−8.6	−6.6	2.7	11.6	12.3	9.3	7.1	−7.8	−9.5	−0.3	11.2	13.1	10.8	9.4
Difference	0.7	0.4	1.2	1.8	1.6	1.7	0.2	5.6	0.7	0.3	0.3	0.3	0.1	0.2	0.3	0.5	0.6	0.1	0.3	0.4	0.3
CF Predicted	−8.0	−6.8	1.7	11.1	13.7	10.3	7.8	−16.8	−8.5	0.4	9.3	10.0	6.8	4.3	−15.8	−17.3	−8.0	2.8	5.1	2.9	1.4
Observed	−8.9	−7.1	0.5	8.0	11.7	9.4	7.1	−11.2	−8.3	0.2	8.5	9.0	6.1	3.8	−16.7	−15.9	−6.9	1.3	3.9	2.2	0.5
Difference	0.9	0.3	1.2	3.1	2.0	0.9	0.7	5.6	0.2	0.2	0.8	1.0	0.7	0.5	0.9	1.4	1.1	1.5	1.2	0.7	0.9

TABLE 2,*B*. THE PREDICTED AND OBSERVED VALUES FOR THE MEAN T DEFLECTIONS

	QRS AXIS 0° TO +34°							QRS AXIS +35° TO +59°							QRS AXIS +60° TO +90°						
	PRECORDIAL POSITION							PRECORDIAL POSITION							PRECORDIAL POSITION						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
V Observed	0.3	3.9	4.8	4.6	3.6	2.8	2.2	1.0	4.7	3.9	4.4	3.5	2.5	2.0	1.3	5.6	5.5	5.0	4.0	2.6	2.2
V_R Observed				−1.7							−1.5							−1.5			
V_L Observed				0.6							0.5							0.3			
V_F Observed				0.8							1.2							1.4			
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
CR Predicted	2.0	5.6	6.5	6.3	5.3	4.5	3.9	2.5	6.2	5.4	5.9	5.0	4.0	3.5	2.8	7.1	7.0	6.5	5.5	4.1	3.7
Observed	1.5	5.2	6.3	5.3	5.0	4.1	3.6	3.1	5.5	6.2	5.7	5.0	4.1	3.4	2.8	6.5	7.3	6.6	5.2	4.1	3.4
Difference	0.5	0.4	0.2	1.0	0.3	0.4	0.3	0.6	0.7	0.8	0.2	0.0	0.1	0.1	0.0	0.6	0.3	0.1	0.3	0.0	0.3
CL Predicted	−0.3	3.3	4.2	4.0	3.0	2.2	1.6	0.5	4.2	3.4	3.9	3.0	2.0	1.5	1.0	5.3	5.2	4.7	3.7	2.3	1.9
Observed	−0.9	3.4	4.3	4.2	3.2	2.3	1.6	1.2	4.4	4.3	3.9	3.1	2.1	1.7	1.7	5.4	5.7	4.7	3.2	2.3	1.9
Difference	0.6	0.1	0.1	0.2	0.2	0.1	0.0	0.7	0.2	0.9	0.0	0.1	0.1	0.2	0.7	0.1	0.5	0.0	0.5	0.0	0.0
CF Predicted	−0.5	3.1	4.0	3.8	2.8	2.0	1.4	−0.2	3.5	2.7	3.2	2.3	1.3	0.8	−0.1	4.2	4.1	3.6	2.6	1.2	0.8
Observed	−1.0	3.2	4.2	3.9	2.7	1.8	1.2	0.0	3.9	3.9	3.3	2.3	1.5	0.9	−0.2	4.5	4.7	3.6	2.3	1.1	0.5
Difference	0.5	0.1	0.2	0.1	0.1	0.2	0.2	0.2	0.4	1.2	0.1	0.0	0.2	0.1	0.1	0.3	0.6	0.0	0.3	0.1	0.3

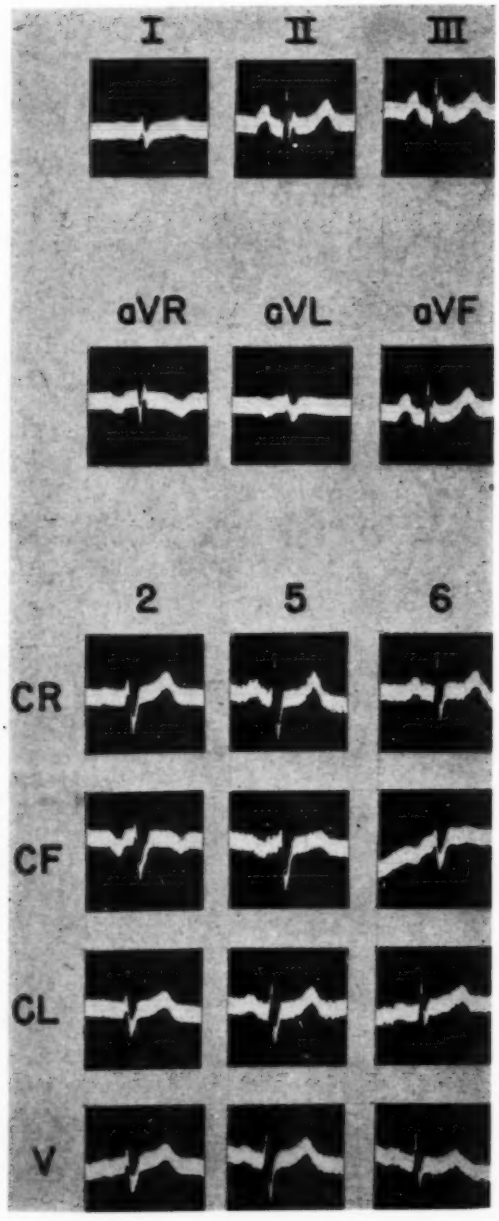

Fig. 1.—A case of pulmonary emphysema showing abnormally small R waves and relatively deep S waves in CF leads indicative of possible right ventricular preponderance; CR, CL, and V leads show normal R/S ratios. Note also T-wave inversion in Lead CF_2 as compared with upright T waves in CR_2, CL_2, and V_2. Note also the inverted P waves in the CF leads, not present in the CR, CL, or V leads. This record is definitely abnormal and shows a P-pulmonale. In a case of this sort it may be properly asked whether the abnormalities in the CF leads are more informative than the absence of such abnormalities in the CR, CL, and V leads.

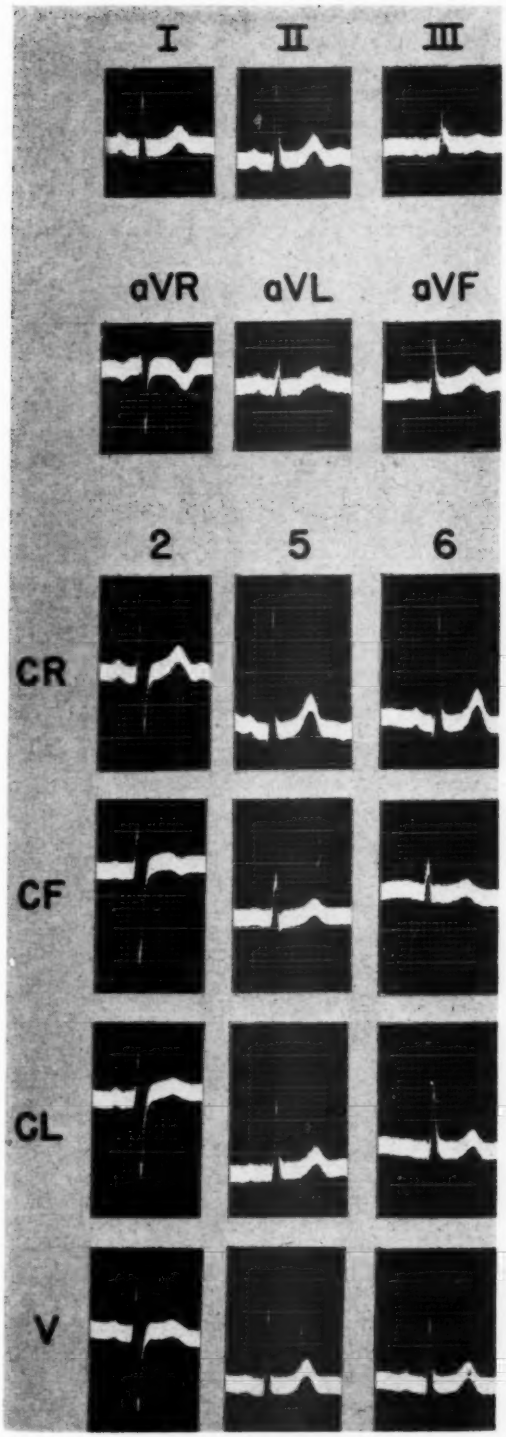

Fig. 2.—An example of an isolated inverted T wave in CF_2 and upright T waves in Leads CR_2, CL_2, and V_2 in a subject with no evidence of heart disease and no other electrocardiographic abnormalities.

2. In CF leads, as the QRS axis shifted from left to right, the P, R, and T waves, in general, decreased in amplitude, and the S waves increased in amplitude (Tables 1,*A*, 1,*B*, and 1,*C*). Changes also occurred in the other leads but were less marked than in CF. Thus, the most conspicuous differences in subjects with right axis shift occurred between CF and the other leads in positions from the left precordium. In left axis shift, the principle differences, but less conspicuous, occurred between CL and the other leads.

3. The predicted and observed values for the mean QRS and T deflections in CR, CL, and CF leads are given in Tables 2,*A* and 2,*B*. The observed values for QRS and T in the V precordial and V extremity leads are also shown. The mean error between the predicted and observed QRS was 1.3 mm. with a range of 0.1 to 5.6 millimeters. The mean error between the predicted and observed T waves was 0.3 mm. with a range of 0.0 to 1.2 millimeters.

4. We have observed four types of electrocardiograms in which the differences between CF and V leads may be sufficient to influence the interpretation of the electrocardiogram:

A. In some subjects with normal right axis shift, or with pulmonary emphysema, CF leads may record QRS complexes which have relatively small R waves and large S waves in precordial Positions 5 and 6. This precordial pattern associated with right axis shift in the limb leads may be suggestive of right ventricular preponderance. V leads (or CR or CL leads) record complexes which have a normal R/S ratio in the positions from the left precordium. An example is shown in Fig. 1.

B. Some normal adults have an inverted T wave in Lead CF_2 as an isolated finding. This may indicate an abnormal electrocardiogram. In some of these cases Lead V_2, CR_2, or CL_2 will record upright T waves. An example is shown in Fig. 2.

C. An occasional subject with normal right axis shift or pulmonary emphysema may show T-wave inversion in CF_6. This would be considered distinctly abnormal, yet V, CR, or CL leads may record upright T waves at the same position. An example is shown in Fig. 3.

The abnormalities listed in A, B, and C sometimes may all occur in the same record.

D. In some patients with healing or healed posterior wall infarction who show inverted T waves in Leads II, III, and V_F and upright T waves in CF leads, V, CR, and CL leads from precordial Positions 5 or 6 may record inverted T waves. Localization of the infarct to the posterolateral wall would be justified from the T-wave inversion in these positions. This localization could be made with V, CR, or CL leads, but not with the CF lead. An example is shown in Fig. 4.

DISCUSSION

The results of our present study confirm the work of Hecht[7] and others, indicating that precordial leads obtained by a chest-extremity method differ, depending on the extremity used, and such leads, in turn, differ from precordial leads using the central terminal as the location for the indifferent electrode.

In general, these differences follow a pattern which can be related to the direction of the QRS axis and the type of complexes recorded from the extremities. Thus, as the QRS axis shifts from left to right, the QRS and T complexes recorded at the left arm change from a mainly upward (plus) to a mainly downward (minus) deflection, and the QRS and T complexes recorded at the left leg change from a mainly downward (minus) to a mainly upward (plus) deflection. The

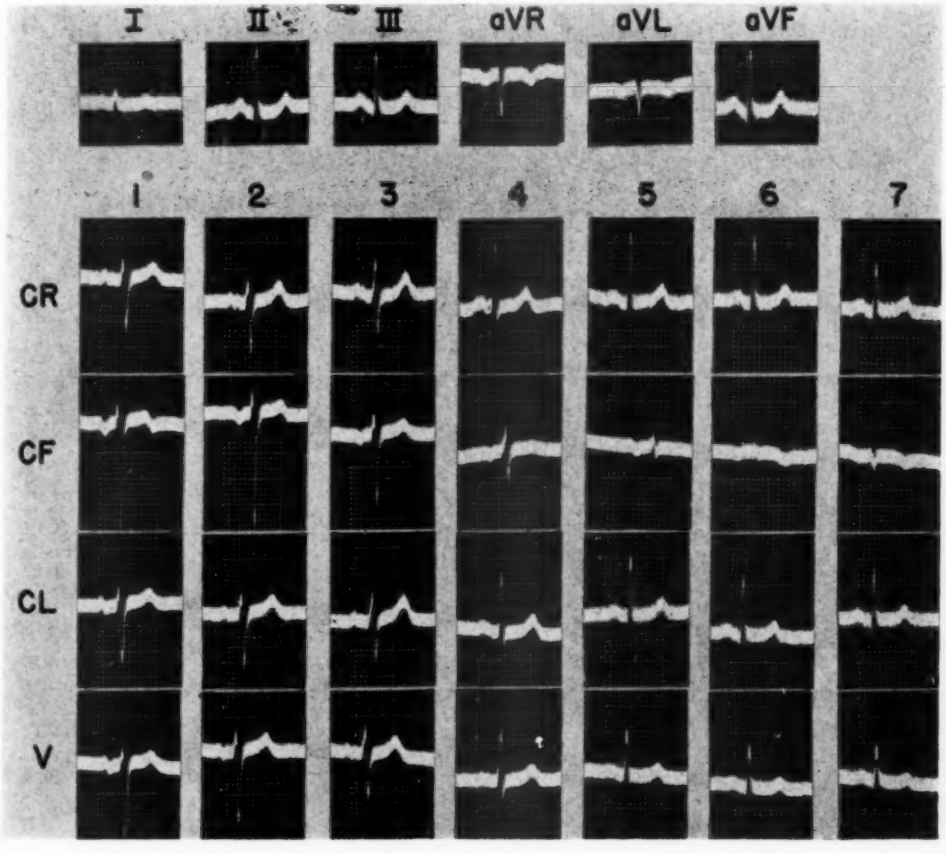

Fig. 3.—A normal subject with right axis shift showing the marked effect produced by the left leg potential in CF leads from the left precordium. There is much less difference between CL, CR, and V leads. Note also the T-wave inversion in Lead CF_6 as compared with upright T waves in CR_6, CL_6, and V_6.

QRS and T complexes recorded at the right arm are normally downward (minus), and vary relatively little with changes in the direction of the QRS axis. It would thus be anticipated that precordial leads obtained with the indifferent electrode, respectively, on the left leg or left arm would vary most with right or left axis shift (Figs. 3 and 5). The results agree for the most part with the prediction. CR and V leads do show variations as the QRS axis shifts, but they are not as conspicuous as in CF or CL leads.

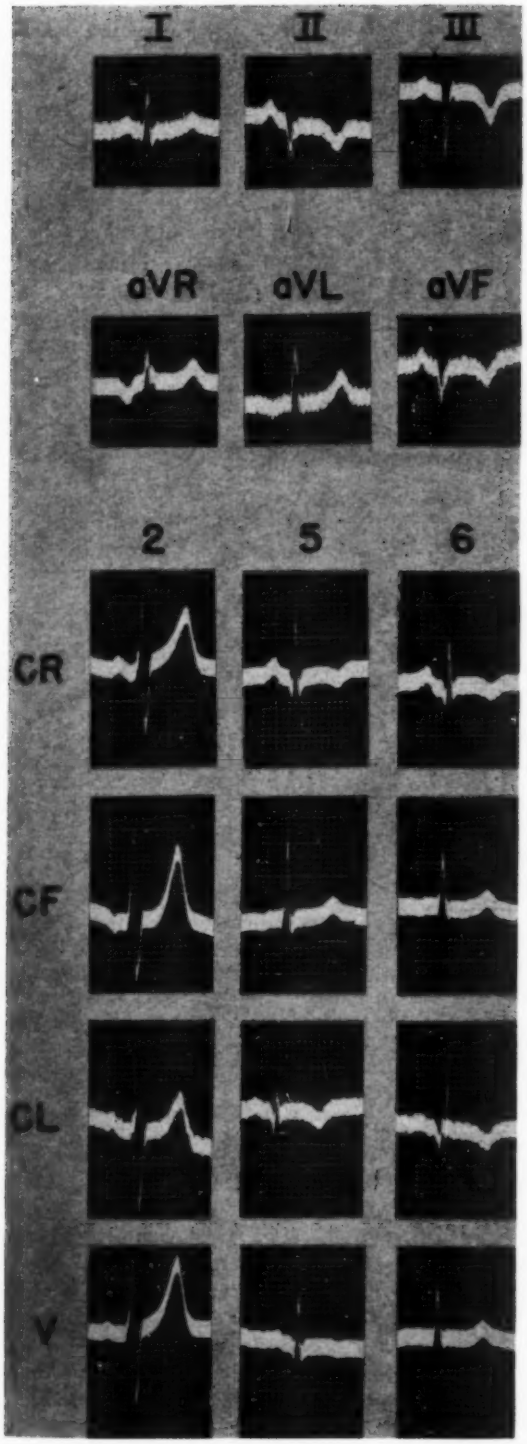

Fig. 4.—An example of myocardial infarction showing a posterior wall pattern in the limb and CF leads and a posterolateral wall pattern in CR, CL, and V leads. Leads CF_5 and CF_6 fail to show the abnormal inverted T waves seen in the CR and CL leads and, to a lesser extent, in V_5.

We have applied to our data, as an assumption, the concept that the central terminal has zero potential, in an attempt to predict accurately the amplitude of the deflections which should be obtained in CR, CL, or CF leads. Since a precordial lead records the difference in potential between the chest electrode and the extremity electrode, and if the central terminal is assumed to be constantly at zero potential, then at a given precordial position at a given instant the algebraic difference between the V precordial lead and the V extremity lead will

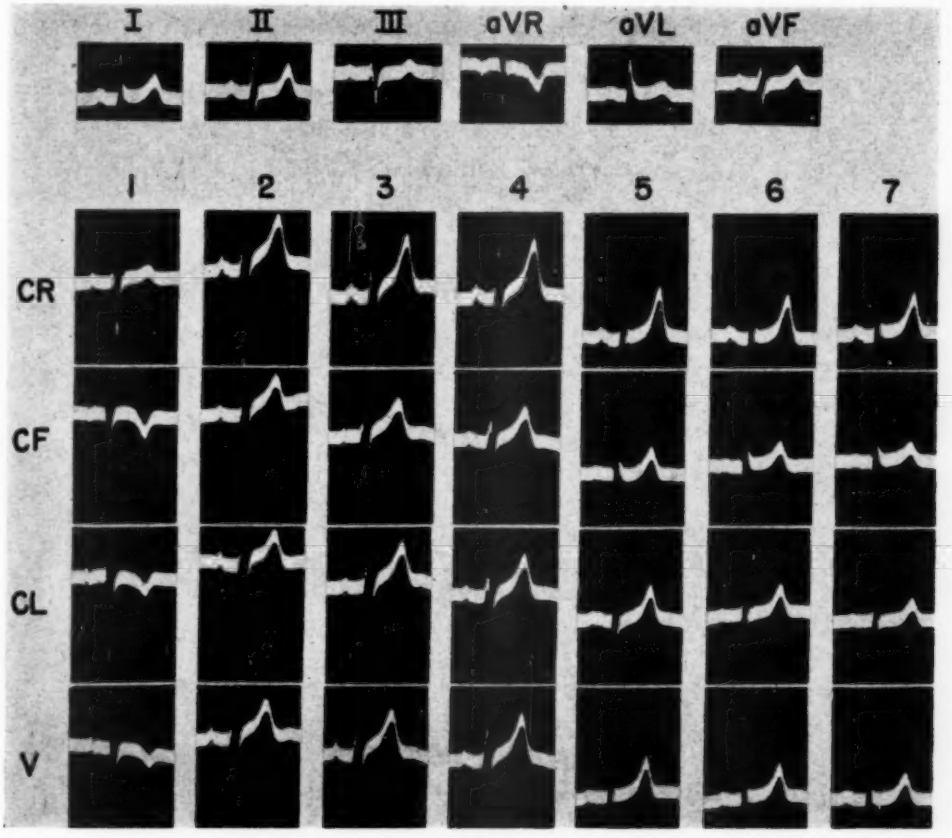

Fig. 5.—A normal subject with left axis shift showing the effect of the left arm potential on CL leads from the left precordium.

equal the precordial lead which has its indifferent electrode located on the particular extremity. The predicted and observed values are listed in Tables 2,*A* and 2,*B*. It is apparent that precise agreement between the predicted and observed values occurs relatively infrequently. Nevertheless, the mean error is small. Part of the error is undoubtedly due to measurement and part must be due to the fact that we did not obtain the precordial and V extremity leads simultaneously. But the fact remains that, with routine methods being employed, the concept that the central terminal is at zero potential does not receive rigid support from the facts. However, we do feel justified in concluding from our

data that it is possible, within a range of error, to use central terminal leads to explain and obviate the different effects exerted by the extremities on precordial leads.

For the purposes of clinical electrocardiography it is probably true that it makes little difference in the vast majority of cases whether the indifferent electrode be placed on the right arm, left arm, left leg, or attached to the central terminal. This is as would be expected since the relatively great distance of the extremity electrode from the heart, as compared with the precordial electrode, tends to minimize the influence of the indifferent electrode. In some cases, examples of which are shown, the differences are sufficient to affect the interpretation. The frequency of such cases in clinical electrocardiography is probably of the order of magnitude of 5 per cent. For the most part, these electrocardiograms show right axis shift and tall QRS complexes in the left leg resulting in small or even inverted QRS deflections in CF leads taken over the left precordium. The variations in the direction of the T wave in precordial Position 2 and the direction of T in Positions 5 or 6 in posterior wall infarction in various types of precordial leads have been pointed out previously.[12,15] It has been shown[12] that CF leads from the left precordium may fail to record prominent Q waves in posterolateral infarction, whereas V leads will record these deflections. In Fig. 4 prominent Q waves are seen only in Leads CL_5 and CL_6. The rare T-wave inversion in CF_5 or CF_6 in normal subjects which appears to be the result of the relatively tall T wave in Lead V_F and which becomes upright in V, CR, or CL leads was postulated by Hecht[7] and illustrated by Alzamora Castro.[12]

It is not possible at present to make a categorical statement as to the ideal location for the indifferent electrode. On theoretical grounds CR, CL, and CF leads are equally undesirable since all are subject to the distorting effects of the potential of the indifferent electrode. The magnitude and variability of the distortion will be most pronounced in CF and CL leads, which directly reflect change in the anatomic position of the heart. It is apparent that when the potential recorded at an extremity is large, its effect on a precordial lead is considerable, and when the extremity potential is small, its effect on a precordial lead is minimal. If the central terminal can be shown to be relatively constant in potential and consistently more indifferent than the extremities, it will be the location of choice, among those available, for the indifferent electrode.

SUMMARY AND CONCLUSIONS

1. A comparison has been made of CR, CL, CF, and V leads recorded at identical precordial positions in forty-four normal subjects and in a group of patients with posterior wall infarction, emphysema, and nonspecific electrocardiographic abnormalities in order to re-evaluate the differences among these leads and to cite instances where the differences may influence the interpretation of the electrocardiogram.

2. In general, the amplitude of the deflections was greatest in CR and smallest in CF leads. The size of the deflections varied with the direction of the QRS axis. This was most marked in CF leads which showed a progressive de-

crease in the R/S ratio as well as an absolute decrease in the size of the R and S waves in leads from the left precordium as the QRS axis shifted from left to right. Similar but less pronounced changes occurred in CL leads as the QRS axis shifted from right to left. CR and V leads remained more constant, but not absolutely so, with changes in the direction of the QRS axis.

3. The differences among CR, CL, CF, and V leads can be explained, with a relatively small mean error, on the basis of the influence of the extremity when the central terminal is used to record the precordial and extremity potentials. Within this range of error it may be said that the substitution of V precordial leads for chest-extremity lead combinations will eliminate the effect of the extremity potential on the precordial electrocardiogram.

4. Four types of electrocardiograms are illustrated: (a) those in subjects with right axis shift or with pulmonary emphysema showing a small R in Leads CF_5 and CF_6 and a normal R/S ratio in V_5 and V_6; (b) those in normal adults with isolated T-wave inversion in Lead CF_2 but not in V_2; (c) those with right axis shift or emphysema with isolated T-wave inversion in CF_6 but not in Lead V_6; and (d) those with healing or healed posterior wall infarction with an inverted T wave in Leads II, III, and V_F associated with an upright T wave in CF leads and an inverted T wave in the V leads. In these the differences between CR, CL, CF, and V leads may be of sufficient magnitude to affect the interpretation of the electrocardiogram. In these examples, the CF lead differs most from the other lead combinations. Such instances occur in about 5 per cent of cases. In the vast majority of cases it probably makes little difference whether the electrode is on the right arm, left arm, left leg, or attached to the central terminal as far as clinical interpertation is concerned.

REFERENCES

1. Wilson, F. N., Johnston, F. D., Macleod, A. G., and Barker, P. S.: Electrocardiograms That Represent the Potential Variations of a Single Electrode, Am. Heart J. **9**:447, 1933.
2. Wilson, F. N., Macleod, A. G., and Barker, P. S.: The Potential Variations Produced by the Heart Beat at the Apices of Einthoven's Triangle, Am. Heart J. **7**:207, 1931.
3. Eckey, P., and Fröhlich, R.: Zur Frage der unipolaren ableitung des Elktrokardiogramms, Arch. f. Kreislaufforsch. **206**:181, 1938.
4. Wilson, F. N., Johnston, F. D., Rosenbaum, F. F., and Barker, P. S.: On Einthoven's Triangle, the Theory of Unipolar Electrocardiographic Leads, and the Interpretation of the Precordial Electrocardiogram, Am. Heart J. **32**:277, 1946.
5. Viana, F. P.: Determinacão Experimental do Potencial do Terminal Central de Wilson, Amatus **5**:133, 1946.
6. Burger, R.: Ueber das Elektrische Feld des Herzens. I. Mitteilung, Cardiologia **3**:56, 1939.
7. Hecht, H. H.: The Influence of the Indifferent Electrode Upon the Precordial Electrocardiogram. I. The Normal Electrocardiogram, Am. Heart J. **24**:529, 1942.
8. Wallace, L., and Grossman, N.: Precordial Electrocardiograms. A Comparison of CF and V Lead Connections, Brit. Heart J. **8**:83, 1946.
9. (a) Groedel, F. M.: How Far Does the Situation of the Indifferent Electrode Influence the Electrocardiographic Unipolar Chest Leads? Cardiologia **3**:23, 1939.
   (b) Groedel, F. M.: How Far is the Unipolar Chest Electrocardiogram Influenced When Led at the Same Time to Two or Three Electrically Connected Extremities? Cardiologia **3**:36, 1939.
   (c) Groedel, F. M.: How Far is the Asynchronism of the R Waves of the Right and Left Electrocardiogram Influenced by Different Placement of the Indifferent Electrode? Cardiologia **3**:49, 1939.

10. Hayos, J. M., and Tomayo, A. G.: Comparative Study of Different Precordial Leads, Am. Heart J. **33**:698, 1947, (Abstract).
11. Deeds, D., and Barnes, A. R.: The Characteristics of the Chest Lead Electrocardiograms of 100 Normal Adults, Am. Heart J. **20**:261, 1940.
12. Alzamora Castro, V.: La influencia de un electrodo no indiferente en el electrocardiogramma precordial, Gac. méd. de Lima **2**:181, 1946.
13. Wolferth, C. C., and Wood, F. C.: The Prediction of Differences Between Precordial Leads CR, CL, and CF. Based on Limb Lead Findings, Am. Heart J. **20**:12, 1940.
14. Goldberger, E.: A Simple, Indifferent Electrocardiographic Electrode of Zero Potential and a Technique of Obtaining Augmented, Unipolar, Extremity Leads, Am. Heart J. **23**:483, 1942.
15. Littman, D.: Persistance of the Juvenile Pattern in the Precordial Leads of Healthy Adult Negroes, With Report of Electrocardiographic Survey on Three Hundred Negro and Two Hundred White Subjects, Am. Heart J. **32**:370, 1946.

NEOSYNEPHRINE IN TREATMENT OF PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA

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MECHANICAL methods of treatment are frequently unsuccessful in stopping attacks of paroxysmal supraventricular tachycardia. In some protracted attacks the effects of the rapid heart action on the circulation are sufficiently serious to justify the use of drugs in an attempt to restore normal rhythm. Quinidine is frequently effective in terminating an attack, but it does so only after a considerable and variable latent period, which makes the therapeutic evaluation of this drug difficult. Mecholyl is likewise often effective in stopping paroxysmal tachycardia, but it produces distressing side effects, which may be more disturbing than the rapid heart action itself.

In a preliminary paper we have reported the efficacy of Neosynephrine in reverting paroxysmal supraventricular tachycardia to normal rhythm.[1] Keys and Violante[2] had studied effects of Neosynephrine in various cardiac arrhythmias, and their report included two cases of paroxysmal auricular tachycardia, which were reverted to normal rhythm.

MECHANISM OF ACTION OF NEOSYNEPHRINE

Neosynephrine differs from epinephrine in that the molecule has a hydrogen atom instead of the hydroxy group in the para position on the benzene ring. In spite of their similarity chemically, the cardiovascular effects of the two drugs are quite different. The potency of Neosynephrine as a direct stimulant to the cardiac conducting mechanism is much less than that of epinephrine,[3] while its potency as a vasoconstrictor is relatively high. Therefore, when Neosynephrine is given to intact animals or man in nontoxic doses, it causes a rise in blood pressure which elicits cardioinhibitory reflexes from the aortic arch and carotid sinuses. These reflex inhibitory influences are more than sufficient to counteract the mild direct stimulating action of Neosynephrine on the sinoauricular node. When relatively large doses of Neosynephrine are given to dogs, the pacemaker may be displaced downward so that a ventricular bradycardia, on an escape basis, results. As the dosage is increased to very high levels, ventricular tachycardia is produced. Intravenous doses of 50 mg. given rapidly to each of several dogs weighing 10 to 12 kilograms produced a multifocal ventricular tachycardia.

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Neosynephrine has an accelerator action on the denervated heart.[3] In this respect it is one twenty-fifth to one fiftieth as potent as epinephrine.

It is considered that Neosynephrine, intravenously, stops paroxysmal supraventricular tachycardia by producing a sudden vasoconstriction which in turn causes a rapid rise in pressure in the aortic arch and carotid sinuses. Consequently, all four afferent pathways concerned with reflex cardiac slowing are simultaneously activated. These buffer reflexes are very sensitive in unanesthetized animals and in man, and only a moderate rise in blood pressure is required to cause considerable cardiac inhibition.

Theoretically, compounds which produce a slower and more prolonged rise in blood pressure than that caused by Neosynephrine would probably be

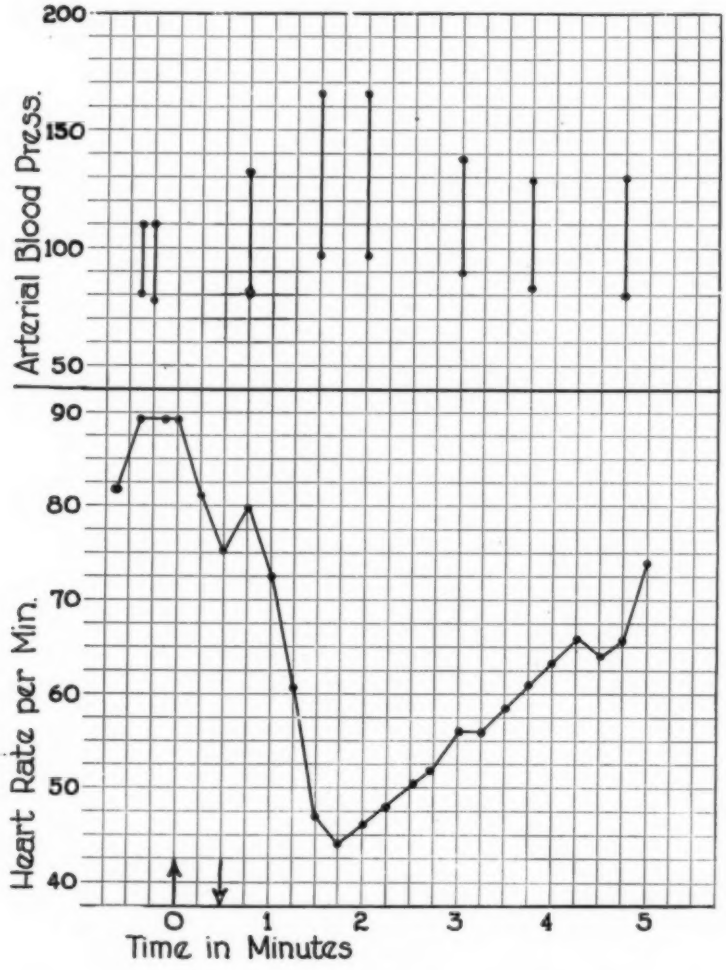

Fig. 1.—Typical changes in heart rate and blood pressure produced by intravenous injection of 0.30 mg. of Neosynephrine during the period of thirty seconds indicated by the arrows. Normal young man.

less effective as cardioinhibitors. Furthermore, administration of Neosynephrine by any route other than the intravenous one is less desirable, for it produces a more gradual, less predictable, and more prolonged rise in arterial pressure.

NEOSYNEPHRINE IN NORMAL HUMAN SUBJECTS

The cardiovascular actions of Neosynephrine in man have been studied by Keys and Violante[2] and by Hecht and Anderson.[4] We have studied effects of rapid intravenous injection of 0.30 mg. of Neosynephrine in seven normal human subjects for the purpose of determining the extent and duration of the changes

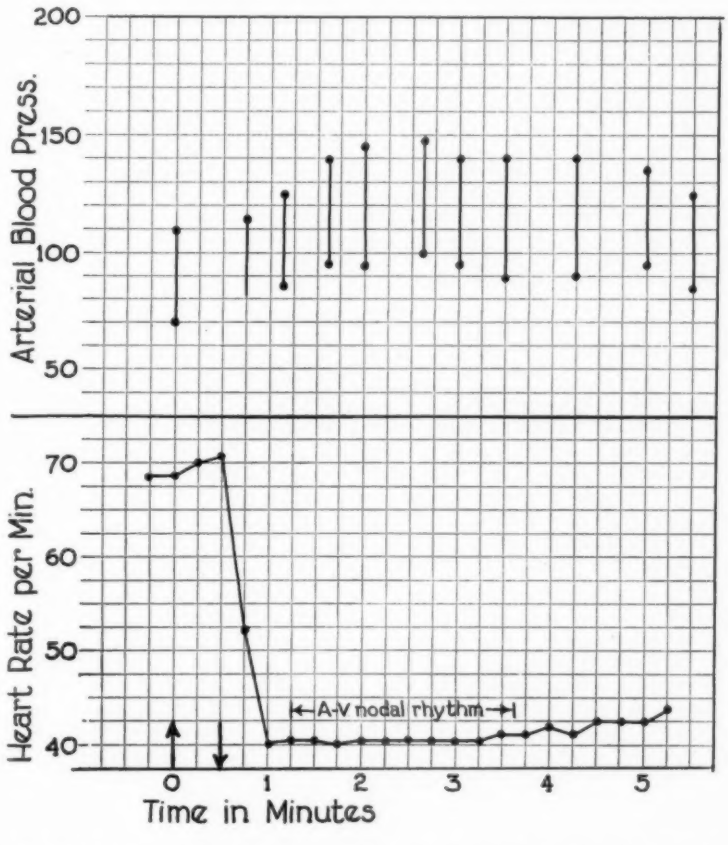

Fig. 2.—Production of a slow A-V nodal rhythm in a normal young man by injection of 0.30 mg. of Neosynephrine during the period of thirty seconds indicated by the arrows.

in blood pressure and heart rate. Continuous electrocardiograms were recorded during each experiment. The Neosynephrine was injected intravenously within twenty to thirty seconds. Forty-five seconds after the beginning of the injection in each case, the systolic and diastolic pressures were noted to be rising and the heart rate decreasing. The extent of the rise in systolic pressure varied considerably in different individuals. The minimal rise produced was 10 mm. Hg

TABLE I. EFFECT OF NEOSYNEPHRINE ON PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA

CASE	AGE	SEX	BLOOD PRESSURE BETWEEN ATTACKS	ATTACK NUMBER	DATE	HEART RATE	SYSTOLIC BLOOD PRESSURE DURING ATTACK	I. V. NEOSYNEPHRINE		
								DOSE (MG.)	MAXIMUM SYSTOLIC PRESSURE PRODUCED (MM. HG)	TIME FROM BEGINNING OF INJECTION TO REVERSAL*
1 J. B.	38	F	155/85	1	12/25/46	185	105	2.5	210	50 sec.
				2	2/17/47	185	125	0.8	202	45 sec.
				3	2/22/47	185	100	0.5 0.8 1.0	130 140 155	U U 70 sec.
				4	10/25/47	208	110	0.8 1.0	144 200	U 60 sec.
				5	11/ 2/47	220	104	0.5	134	75 sec.
				6	11/18/47	190	110	5.0	210	40 sec.
2 K. H.	51	F	140/90	1	1/22/47	165	110	0.3 0.6 0.8	140 150 160	U U 45 sec.
				2	3/15/47	176	146	0.8 1.0	210 218	U 70 sec.
3 G. M.	20	F		1	1/31/47	170	110	0.4	140	45 sec.
4 I. H.	44	M	130/84	1	2/13/47	210	80	0.8	120	45 sec.
5 P. F.†	45	F	120/70	1	2/15/47	180	104	0.5 1.0 1.5 1.9	120 135 145 156	U U U U

6	S. G.†	53	F	190/100	1	2/19/47	150-164	90	0.3 0.5 0.5 0.8	115 120 150 170	U U U U
7	M. S.	65	F	180/110	1	3/28/47	166	110	1.0	Not taken	60 sec.
9	A. B.	59	F	110/68	1	5/26/47	160	76	10.0	Not taken	less than 60 sec.
10	A. W.	28	M	120/76	1	7/12/47	170	96	0.5	142	35 sec.
					2	7/30/47	168	84	0.5	136	45 sec.
					3	8/13/47	220	98	0.5	133	62 sec.
					4	10/16/47			0.5		less than 60 sec.
					5	10/23/47			0.5		less than 60 sec.

Case 8—Ventricular tachycardia, therefore not included in this table.
*U = unsuccessful.
†Postoperative

and the maximal was 50 mm. of mercury. The diastolic pressure rose less than the systolic. The maximal pressure was attained during the period ninety to one hundred fifty seconds after the beginning of the injection. The heart rate began to decrease precipitously during the period from thirty to ninety seconds after the drug was given and reached the lowest level, usually in the range from 40 to 56 beats per minute, ninety to one hundred fifty seconds from the beginning of the injection. Blood pressure and heart rate gradually returned to the preinjection level within seven to ten minutes after the drug was administered.

Data from two of these records are shown graphically in Figs. 1 and 2. In Fig. 1 a typical response is illustrated. Occasionally the pacemaker is displaced so that an auriculoventricular nodal rhythm is produced as indicated in Fig. 2.

TERMINATION OF ATTACKS OF PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA WITH NEOSYNEPHRINE

We have data on the use of Neosynephrine in the treatment of nineteen attacks of paroxysmal supraventricular tachycardia. The drug produced reversion to the normal rhythm in seventeen attacks in seven patients. It failed in two cases in which the attacks developed following major surgical procedures. The results are summarized in Table I, and brief case histories are presented below.

CASE 1.—J. B., a 38-year-old white woman, had experienced frequent attacks of paroxysmal auricular tachycardia for ten years. The episodes lasted from fifteen minutes to several hours and had become increasingly more difficult to stop. Her blood pressure between attacks ranged from 155/85 to 120/80. Previously she had controlled her attacks with hypnotics, and, following a sound sleep, she would usually awaken with a normal rhythm. Carotid sinus massage was never effective. Since 1944 attacks had been controlled successfully with Mecholyl. More recently larger doses of this drug were found necessary to stop the attacks, and gastrointestinal side effects were very disturbing.

On Dec. 25, 1946, at 11:00 A.M. she developed persistent tachycardia which did not respond to 100 mg. of Mecholyl, 15 mg. of morphine sulfate, 180 mg. of intravenous sodium amytal, and 90 mg. of Nembutal by mouth, all given over a period of four hours. Carotid sinus massage and ocular pressure were also ineffective. At 6:30 P.M. her heart rate was 185 per minute and her blood pressure 105/80. Neosynephrine, 2.5 mg., was given intravenously. The systolic pressure rose to 160 mm. Hg within fifty seconds, at which time the tachycardia terminated abruptly. The systolic pressure continued to rise to 210, and the patient experienced mild transitory precordial discomfort. The blood pressure returned to the preinjection level in four minutes.

On Feb. 17, 1947, she was again seen with a heart rate of 185 and systolic pressure of 128 mm. of mercury. The attack had been in progress for two hours. Neosynephrine, 0.8 mg., intravenously, produced a rise of the systolic arterial pressure to 198 mm. Hg, and a normal sinus rhythm appeared forty-five seconds after the injection of the drug was begun (Fig. 3).

On Feb. 22, 1947, the patient was seen one hour after the onset of another attack of tachycardia. Her systolic pressure on this occasion was 100 mm. of mercury. A dose of 0.5 mg. of Neosynephrine caused a rise in systolic pressure to 130, but did not revert the tachycardia. Because of precordial pain radiating to the left arm, which she frequently had with attacks, she was given nitroglycerin, 0.4 mg., under the tongue. Ten minutes later Neosynephrine, 0.8 mg., raised the systolic pressure only to 130. It was concluded that the absence of an effective pressure rise was due to the nitroglycerin. Thirty minutes later 1.0 mg. of Neosynephrine given intravenously raised the systolic pressure to 155 mm. Hg, and in seventy seconds the rhythm reverted to normal (Fig. 4).

On Oct. 25, 1947, the patient was seen again with tachycardia. Neosynephrine, 0.8 mg., produced a rise of systolic pressure to 144 but did not stop the attack. Ten minutes later the tachycardia yielded to 2.0 mg. of Neosynephrine, which raised the systolic pressure to 200 mm. of mercury. On Nov. 2, 1947, a fifth attack was reverted with 0.5 mg. of Neosynephrine, which produced a systolic pressure of 134 mm. Hg in seventy-five seconds.

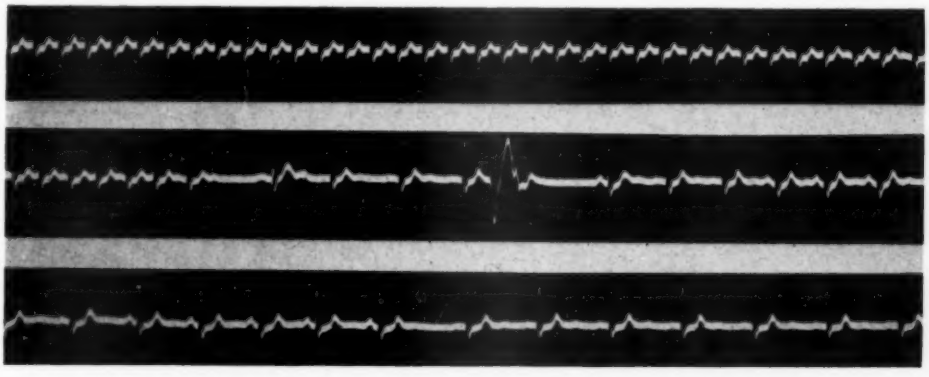

Fig. 3.—Continuous electrocardiographic record showing reversal of paroxysmal supraventricular tachycardia with Neosynephrine. Case 1, second attack.

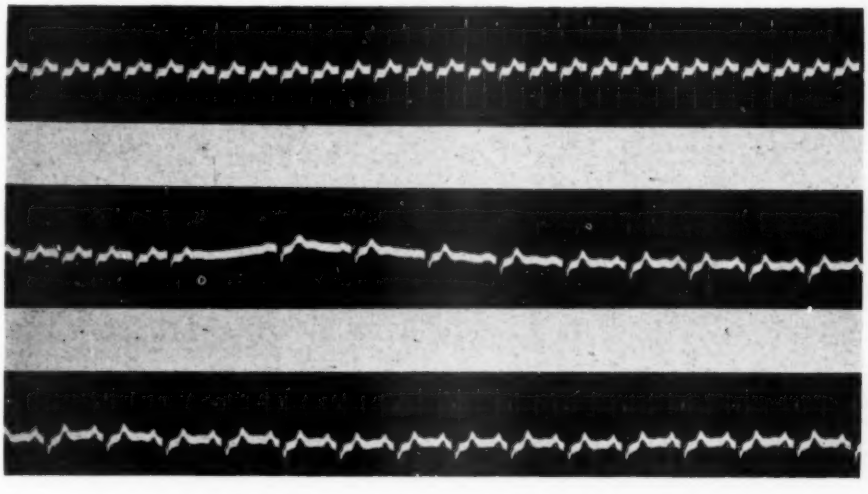

Fig. 4.—Reversal of paroxysmal supraventricular tachycardia with Neosynephrine. Case 1, third attack.

On Nov. 18, 1947, she was again seen in an attack of tachycardia. She was given, by error, 5.0 mg. of Neosynephrine intravenously! Her rhythm returned to a normal sinus mechanism in forty seconds. Sixty seconds after the injection was started, she complained of a violent headache which persisted for fifteen minutes. Her systolic blood pressure rose to 210 mm. Hg and possibly higher. Its peak was not recorded. After fifteen minutes, her pressure had returned to the preinjection level. No untoward effects other than headache were noted following this excessive dose.

CASE 2.—K. H., a 51-year-old white woman, had her first attack of paroxysmal auricular tachycardia in 1911. This episode lasted fifteen minutes and terminated spontaneously. She was then free of attacks until 1941, when they recurred at a frequency of two or three per week. They were controlled with quinidine sulfate, from 90 to 180 mg. daily, and did not recur until 1943 when drug therapy was discontinued. Since 1943 she has had twelve attacks, each lasting from eight to twelve hours, and characterized by precordial pain radiating into the left arm. Her blood pressure between attacks has averaged 140/90.

On Jan. 22, 1947, she was seen in an attack which had lasted thirty-one hours and which had not responded to carotid sinus massage and ocular pressure. Mecholyl, 25 mg., likewise was ineffective and caused nausea, vomiting, and uterine cramps. Her heart rate was 165 per minute and her systolic pressure was 110 mm. of mercury. Increasing doses of Neosynephrine were given intravenously at intervals of ten minutes until the blood pressure was raised sufficiently to stop the attack. The pressure dropped to the preinjection level in each case before the next dose was given. Neosynephrine, 0.3 mg., raised the systolic pressure to 140; 0.6 mg. raised the systolic pressure to 150 mm. of mercury. No effect on the rhythm occurred. When 0.8 mg. of Neosynephrine was given intravenously, the systolic pressure rose to 160 and the tachycardia reverted to a normal sinus rhythm forty-five seconds after the beginning of the injection.

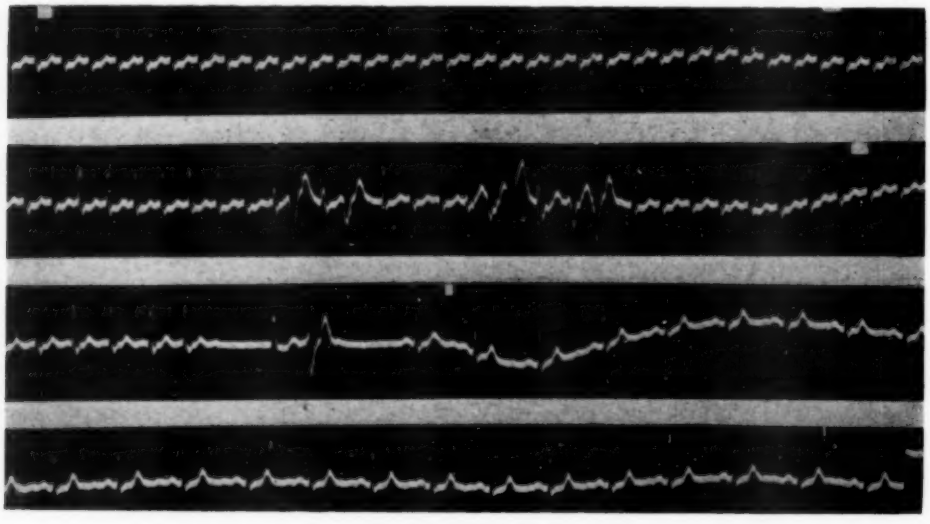

Fig. 5.—Effects of Neosynephrine on supraventricular tachycardia. Case 2, second attack. Explanations in text.

In March, 1947, she was again seen with a heart rate of 176 per minute and a blood pressure of 146/102. Neosynephrine, 0.8 mg., raised the systolic pressure to 210 in sixty seconds and caused the appearance of several ventricular beats, as illustrated in Fig. 5, but the tachycardia continued. Neosynephrine, 1.0 mg., raised the systolic pressure to 214 mm. Hg in seventy-one seconds, and the rhythm abruptly reverted to normal.

CASE 3.—G. M., a 20-year-old white woman, had had three previous short attacks of paroxysmal tachycardia since February, 1946. On Jan. 31, 1947, she had a heart rate of 170 per minute and a systolic pressure of 110 mm. Hg which had been present four hours and persisted in spite of carotid sinus massage and ocular pressure. Electrocardiographic tracings were typical of a nodal tachycardia. Neosynephrine, 0.4 mg., intravenously, raised the systolic pressure to 140 mm. Hg and the tachycardia abruptly reverted to normal sinus rhythm forty-five seconds after the start of the injection (Fig. 6). In this instance a brief paroxysm of ventricular tachycardia preceded the reversion.

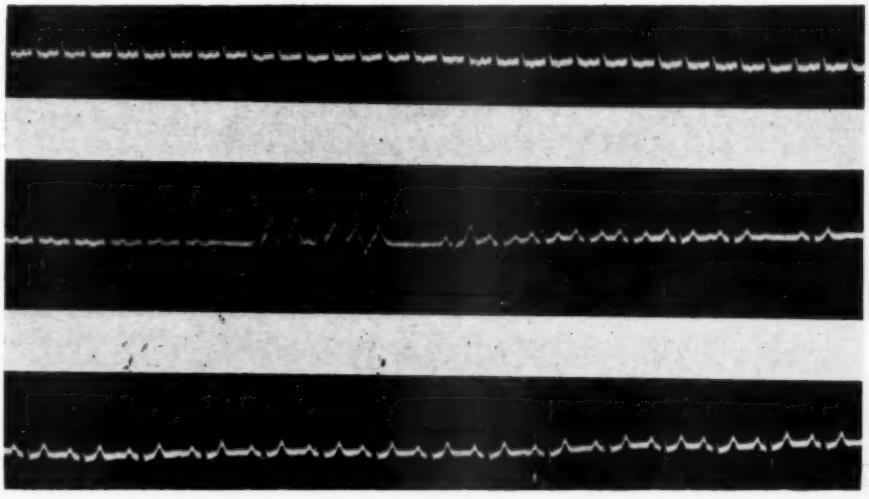

Fig. 6.—Reversal of paroxysmal supraventricular tachycardia with Neosynephrine. Case 3, first attack.

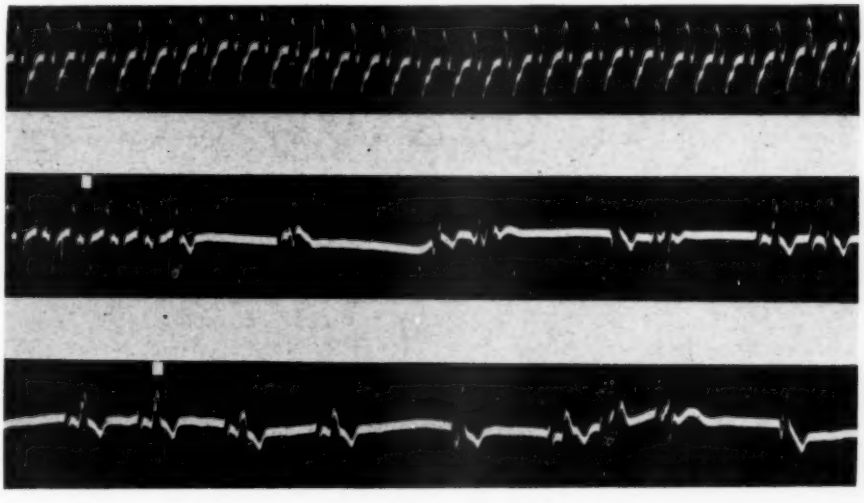

Fig. 7.—Continuous electrocardiographic record, esophageal lead, showing reversal of paroxysmal supraventricular tachycardia with Neosynephrine. Case 4, first attack.

CASE 4.—I. H., a 44-year-old white man, had had paroxysmal auricular tachycardia since 1912. In 1937 he discovered that forcing his breath against a closed glottis often abruptly terminated the attack. In 1946 his spells of tachycardia increased in frequency and were not affected by small doses of digitalis or quinidine. His normal blood pressure was 130/84.

On Feb. 13, 1947, he was seen with a heart rate of 210 and a systolic pressure of 80 mm. of mercury. The tachycardia had persisted for three days, except when it was stopped for a few minutes at a time by the Valsalva maneuver. Neosynephrine, 0.8, 1.0, and 1.2 mg., was given intravenously, in successive doses with no effect on the tachycardia. The vial from which the drug was taken was of the rubber-stoppered type, had been tapped many times, was old, and had been carried in a warm coat pocket for a number of days. A fresh glass ampule of the Neosynephrine

was obtained and 0.8 mg. of the drug from this source was injected. The systolic pressure abruptly rose from 80 to 120 mm. Hg, and the tachycardia reverted to a normal sinus rhythm forty-five seconds after the start of the injection (Fig. 7). The arrhythmia recurred again twenty minutes later. The patient was given quinidine sulfate, 180 mg. every three hours. During the next forty-eight hours he had only four attacks of tachycardia, each lasting less than one hour.

CASE 5.—P. F., a 45-year-old white woman, had had one to four attacks of paroxysmal auricular tachycardia each year since her youth. Exercise or bending over seemed to precipitate the rapid rhythm. These attacks would last only a few minutes and would terminate spontaneously when she would lie down. Her blood pressure normally was 120/70.

On Feb. 15, 1947, a hysterectomy was performed for a fibroid uterus. The hemoglobin was only 64 per cent before surgery. She tolerated the surgical procedure well, and her immediate postoperative course was uneventful. Thirty-six hours postoperatively an attack of tachycardia occurred, lasted four hours, and terminated during gaseous eructation. Two hours later tachycardia recurred, lasted five hours, and terminated spontaneously. The arrhythmia recurred for the third time at 11:00 A.M., Feb. 17, 1947. The heart rate was 180 per minute during this episode and was not affected by carotid sinus massage or ocular pressure. Beginning at 1:40 P.M., Neosynephrine was administered in increasing doses at intervals of ten minutes. The final dose of 1.9 mg. raised her systolic blood pressure from 104 to 156 and was without apparent effect on the heart rate. After four hours the attack terminated during gastric aspiration.

CASE 6.—S. G., a 53-year-old white woman, gave a history of numerous attacks of paroxysmal auricular tachycardia, the longest attack lasting five hours. Her usual blood pressure was 190/100.

On Feb. 19, 1947, during the performance of a cholecystectomy, it was noted that a ligature had been placed about the hepatic artery. The ligature was quickly removed. The artery had not been severed, and the operation was completed. When the patient left the operating table, her blood pressure was 100/70.

Twelve hours postoperatively she was observed to be in shock. Systolic blood pressure was 90. The skin was pale and cold; the heart rate was rapid, varying from 150 to 164 per minute. Because of the variability in the rate, the diagnosis of paroxysmal tachycardia was in doubt until the electrocardiogram was recorded. Neosynephrine, 0.5 mg., was given intravenously and raised the systolic pressure to 120. There was no appreciable effect on the heart rate. Five hundred cubic centimeters of plasma were administered. Shortly thereafter, 0.5 mg. of Neosynephrine raised the systolic pressure to 150, but only very slight transient slowing of the heart rate was observed. A final dose of 0.8 mg. of the drug elevated the systolic pressure to 170, but the tachycardia continued. Quinidine sulfate, 360 mg., was given rectally and repeated three hours later. One hour after the second dose, the heart rate dropped abruptly to 84 per minute, and the tachycardia did not recur.

CASE 7.—M. S., a 65-year-old white woman, had noticed attacks of paroxysmal auricular tachycardia for two and one-half years. The episodes occurred approximately two times per week and usually could be terminated by breath holding. Her blood pressure between attacks ranged from 180/110 to 218/118. Quinidine sulfate, 180 mg., twice daily, did not reduce the frequency of attacks.

On March 28, 1947, she was seen in an attack of tachycardia of six hours' duration that would not yield to the Valsalva maneuver, 180 mg. of quinidine sulfate, carotid sinus massage, or ocular pressure. The heart rate was 166 and the blood pressure was 110/80. Neosynephrine, 1.0 mg., was injected slowly over a period of three minutes, and the systolic pressure was raised to 140. This was without effect on the tachycardia. Thirty minutes later the same dose, 1.0 mg., was given rapidly in less than thirty seconds, and the tachycardia terminated sixty seconds after the start of the injection. Unfortunately, the blood pressure was not recorded at the time of the return to normal rhythm.

CASE 8.—R. R., a 55-year-old white man, suffered an attack of myocardial infarction in 1946. An episode of paroxysmal tachycardia occurred on April 27, 1947. During this attack the heart rate was 168 and the blood pressure was 94/62. The arrhythmia was not reverted by carotid

sinus massage, digitalis, or quinidine. When he was studied on May 10, 1947, his tachycardia had persisted for two weeks. He was given gradually increasing doses of Neosynephrine intravenously. The largest dose was 2.0 mg. and raised the systolic blood pressure only to 130 mm. of mercury. No change in the rhythm was observed on the electrocardiogram. Subsequently it was shown by the use of an esophageal lead that the tachycardia was ventricular in character (Fig. 8).

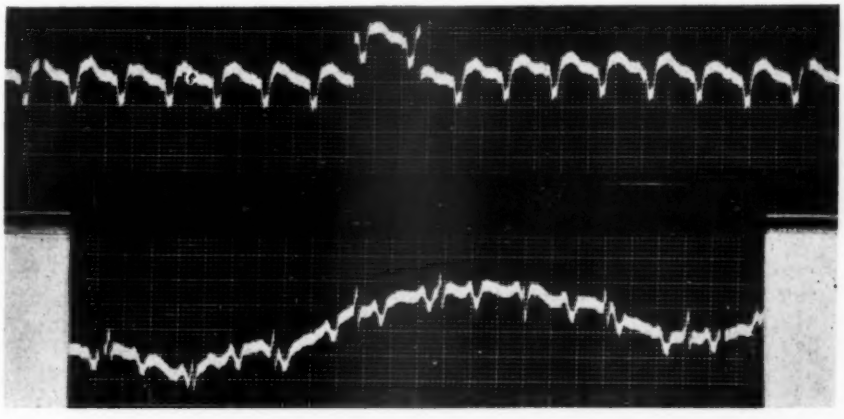

Fig. 8.—Case 8. Ventricular tachycardia. Upper record shows Lead I in which P waves are obscured; therefore, the arrhythmia could be interpreted either as a ventricular tachycardia or as a supraventricular tachycardia with a ventricular conduction defect. Lower record is from an esophageal lead which clearly shows a ventricular rate of 168 and an auricular rate of 96.

CASE 9.—A. B., a 59-year-old white woman, had noted paroxysmal auricular tachycardia since the age of 18 years. The attacks occurred rarely at first but had increased to two per month since 1944. Frequently during attacks she had precordial pain radiating to the left shoulder and arm; this pain had been treated freely with nitroglycerin.

On May 26, 1947, she was seen within an hour after the onset of tachycardia. The heart rate was 160 per minute and the systolic blood pressure was 76. Her usual blood pressure was 110/68. Neosynephrine, 10 mg., was injected intravenously. This excessive dose was the result of a miscalculation. Marked pain in the head and back of the neck occurred, and this was associated with severe agitation. The blood pressure was not recorded. The electrocardiogram showed a brief period of asystole, then numerous ectopic ventricular systoles superimposed on a sinus bradycardia. After ten minutes there was a regular sinus rhythm with a rate of 60 beats per minute.

CASE 10.—A. W., a 28-year-old white man with tuberculosis of the lungs and spine and a tracheomediastinocutaneous fistula, had experienced one episode per month of paroxysmal auricular tachycardia since February, 1946. The attacks lasted from fifteen minutes to several hours and previously had responded to carotid sinus massage. His usual blood pressure ranged from 110/70 to 120/76. In March, 1947, he was digitalized without significant reduction of the frequency of attacks.

On July 12, 1947, he had a heart rate of 170 and a blood pressure of 96/70. This attack had persisted for six hours in spite of repeated attempts to stop it with carotid sinus massage and ocular pressure. Neosynephrine, 0.5 mg., elevated his blood pressure to 142/92 and his tachycardia abruptly terminated thirty seconds after the beginning of the injection. Quinidine sulfate, 180 mg., three times per day, was started and digitalis was discontinued.

On July 30, 1947, another attack began at 4:00 A.M. The heart rate was 168 and the blood pressure was 84/64. At 7:00 A.M. Neosynephrine, 0.5 mg., raised his blood pressure to 136/86

and normal sinus rhythm was restored forty-five seconds after the start of the injection. On Aug. 13, 1947, at 2:00 P.M. an attack of paroxysmal auricular tachycardia again responded to Neosynephrine, 0.5 mg., which elevated the blood pressure to 133/96 in sixty-two seconds.

Two recurrences on October 16 and October 23 would not respond to carotid sinus massage and were terminated by 0.5 mg. of Neosynephrine. Quinidine sulfate, 180 mg., three times per day, had been maintained since July 12.

DISCUSSION

Degree of Rise in Blood Pressure Required to Revert Tachycardia to Sinus Rhythm.—The extent of the rise in blood pressure produced by intravenous Neosynephrine is variable. A dose of 0.5 mg. is a suitable initial trial dose in the typical case. This amount will in some cases terminate the arrhythmia; in others it is insufficient but will serve to assay the patient's pressor response to Neosynephrine. In some of the cases the rhythm was reverted to normal by only enough Neosynephrine to increase the blood pressure suddenly from the subnormal level seen during the attack up to the patient's normal level. This suggests that, in such cases, the low blood pressure secondary to the tachycardia may be an important factor in the perpetuation of the attack. In Case 2 it was necessary to increase the systolic blood pressure to above 200 mm. Hg to stop the arrhythmia. In this case mechanical measures and Mecholyl (25 mg. subcutaneously) were unsuccessful. In Case 1 the doses of Neosynephrine used in the treatment of the first two attacks were greater than necessary, and although the systolic pressure rose to over 200 mm. Hg, the arrhythmia reverted when the systolic pressure reached 160 mm. of mercury. Thus, twelve of the nineteen attacks treated were reverted at a systolic pressure of 160 mm. Hg or less. In two of the cases, data concerning the maximal systolic pressures produced were not obtained. In Case 9, by mistake, twenty times the proper initial dose was given. The paroxysmal auricular tachycardia reverted to ventricular bradycardia and then shortly returned to a normal sinus rhythm. Fortunately, no serious effects resulted.

Time of Reversion.—In each case a suitable amount of Neosynephrine was diluted so that it could be injected conveniently in a period of twenty to thirty seconds. The appearance of normal sinus rhythm occurred during the period of thirty-five to seventy seconds from the beginning of the injection during the time when the systolic blood pressure was rapidly rising.

If reversion of the tachycardia does not occur after a given dose of Neosynephrine, a larger dose may be used any time after the blood pressure has returned to the preinjection level. This has required not longer than ten minutes in the cases studied.

Side Effects.—Amounts of Neosynephrine which are sufficient in the majority of cases to revert paroxysmal supraventricular tachycardia to normal sinus rhythm produce no unpleasant symptoms. "Tingling" or "coolness" of the skin have been noted by most of the patients. Presumably, this is due to the cutaneous vasoconstriction and pilo-erection. A sensation of "fullness of the head" may be produced, and headache may be caused by excessive doses. Transitory pre-

cordial pain has been noted following moderate doses in patients who have complained previously of this symptom during attacks of tachycardia.

Effects in Refractory Cases.—Most of the attacks reverted by Neosynephrine had failed to respond to carotid sinus massage or to ocular pressure. Some of the attacks had persisted in spite of large doses of Mecholyl. The only failures with Neosynephrine were in two patients who developed attacks postoperatively. In Case 5 the maximum systolic pressure produced was 156 mm. Hg; it is quite possible that a larger dose would have reverted the attack. In Case 6 an increase in the pressor action of Neosynephrine after the blood volume was increased by the administration of plasma was demonstrated. A maximal systolic pressure of 170 mm. Hg was produced without affecting the arrhythmia. However, this patient normally had a blood pressure of 190/100, and it is possible that restoration of this level would have resulted in reversion.

Conditions Altering the Cardioinhibitory Response to Neosynephrine.—As would be expected, Neosynephrine is less effective as a pressor agent when the blood volume is low. This was observed in one of our cases when the same dose of Neosynephrine was given before and after transfusion. Doses of Neosynephrine as high as 5.0 mg. have been given intravenously to patients in shock,[5] and the only response noted was minor elevation in blood pressure. It appears that the maximal dose of Neosynephrine which can be given safely is determined by the degree of rise in blood pressure. It is to be expected that Neosynephrine will not revert paroxysmal tachycardia in the occasional cases in which it fails significantly to elevate the blood pressure.

The pressor action of Neosynephrine may be counteracted by previous administration of vasodilator drugs. Adrenolytic drugs would be expected to block its vasoconstrictor action. Heavy doses of barbiturates produce vasodilatation and decrease the sensitivity of the carotid sinus reflexes. Some drugs, such as morphine and neostigmine, sensitize carotid sinus cardioinhibitory reflexes. Therefore, previous administration of these drugs would not be expected to interfere and might increase the effectiveness of Neosynephrine in paroxysmal supraventricular tachycardia. It is obvious that the effects of Neosynephrine cannot be evaluated adequately when the patient is under the influence of various other drugs.

Relative Contraindications to Neosynephrine.—The doses of Neosynephrine which are used to revert paroxysmal supraventricular tachycardia frequently produce ventricular extrasystoles, and occasionally produce a brief paroxysm of ventricular tachycardia at the time of the reversion. Large doses of the drug have a direct stimulatory action on the ventricles, but the extrasystoles seen with small doses may be on a ventricular escape basis or they may, perhaps, be initiated by the sudden change in pressure in the ventricles. We have seen, in experimental animals, that various pressor compounds produce extrasystoles during the rise in blood pressure, even though some of the compounds, such as Pitressin, have no direct stimulatory action on the ventricles. Moreover, huge doses of Neosynephrine do not produce ventricular fibrillation in dogs. However, an increased ventricular irritability may, perhaps, be considered as constituting a

relative contraindication to the use of Neosynephrine intravenously; and, since cardioinhibitory reflexes may not be utilized to influence a ventricular focus, there is less rationale for the use of Neosynephrine in the treatment of ventricular tachycardia. The possibility may be considered that in an occasional instance ventricular tachycardia could be caused by a local effect of sympathetic activity and that this activity could be reflexly depressed following Neosynephrine injection. In this study it was given to one patient with ventricular tachycardia (Case 8). A dose of 2.0 mg. did not produce the expected degree of rise in the blood pressure, and there was no effect on the arrhythmia. In view of the facts just stated, as a general rule the supraventricular origin of the tachycardia should be established before Neosynephrine is used.

A ventricular conduction defect not infrequently becomes evident during an attack of paroxysmal supraventricular tachycardia. When only the standard leads are used in such cases, the electrocardiographic record may resemble that seen in ventricular tachycardia. The differentiation between the two types of arrhythmia can be made by the use of an esophageal lead in which the large auricular deflections are more easily identified.[6] Records obtained by esophageal leads are illustrated in Fig. 7 and the lower portion of Fig. 8.

The presence of hypertension during the tachycardia, or evidence of considerable impairment of coronary circulation, may also be considered as relative contraindications to the use of Neosynephrine intravenously.

SUMMARY

Neosynephrine restores the normal sinus rhythm within thirty-five to seventy seconds after rapid intravenous injection in most cases of paroxysmal supraventricular tachycardia. The reversion of the supraventricular tachycardia is attributable to reflex cardiac inhibition elicited by the rapid rise in pressure in the carotid sinuses and aortic arch. The rise in pressure occurs as a result of the vasoconstriction produced by Neosynephrine. Presumably, any vasoconstrictor compound which acts quickly and briefly, and which has little or no direct stimulating action on the cardiac conducting system, would revert paroxysmal supraventricular tachycardia.

Neosynephrine reverted paroxysmal supraventricular tachycardia in most cases when the systolic pressure reached a level of 160 mm. Hg or less. Some of the attacks which were terminated were refractory to treatment by mechanical methods and by various drugs. In occasional cases reversion was produced with Neosynephrine only when the systolic pressure was elevated to levels which might be considered too high for safety.

In the typical case the rise in systolic blood pressure is proportional to the dose of Neosynephrine, and the maximum dose to be used is determined by the maximum rise in pressure which is considered safe for the individual patient. The initial dose should not exceed 0.5 mg., and any subsequent dose is selected on the basis of the pressor response to the initial dose. Most attacks were reverted by 1.0 mg. or less.

These studies suggest that intravenous injection of Neosynephrine, or some other rapid-acting vasopressor substance, will prove to be the treatment of choice in selected cases of paroxysmal supraventricular tachycardia.

REFERENCES

1. Youmans, W. B., Goodman, M. J., and Gould, Jarvis.: Treatment of Paroxysmal Auricular or Nodal Tachycardia With the Vasopressor Drug, Neosynephrine, Proc. Soc. Exper. Biol. & Med. **64**:380, 1947.
2. Keys, A., and Violante, A.: The Cardio-circulatory Effects in Man of Neosynephrine, J. Clin. Investigation **21**:1, 1942.
3. Youmans, W. B., Haney, H. F., and Aumann, K. W.: Relation of the Groups of the Adrenaline Molecule to Its Cardio-accelator Action, Am. J. Physiol. **130**: 190, 1940.
4. Hecht, Hans H., and Anderson, R. B.: The Influence of Dibenamine (N, N-dibenzyl-β-chloroethylamine) on Certain Functions of the Sympathetic Nervous System in Man, Am. J. Med. **3**:3, 1947.
5. Johnson, Carl.: A Study of Neo-Synephrin Hydrochloride in the Treatment of Acute Shock From Trauma or Hemorrhage, Surg. Gynec. & Obst. **63**:35, 1936.
6. Butterworth, J. Scott, and Poindexter, C. A.: The Esophageal Electrocardiogram in Arrhythmias and Tachycardias, AM. HEART J. **32**:681, 1946.

VII. CORRELATION OF ELECTROCARDIOGRAPHIC AND PATHOLOGIC FINDINGS IN LATERAL INFARCTION

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IT IS well known that the Q_1T_1 pattern customarily attributed to anterior infarction is actually a manifestation of the continuation of the lesion into the lateral wall, and results from the transmission of the potential variations of the epicardial surface of the lateral wall into the axilla and thence to the left arm.[1,2,3,4] The diagnosis of the lateral portion of the anterolateral infarct is much more readily made from Leads V_5 and V_6 and aV_L in such cases and an associated involvement of the anteroseptal wall is revealed by the QRS pattern in the first four precordial leads.[1,2,4] Furthermore, QRS-T abnormalities in Lead I may occur in association with a Q_3T_3 pattern as a manifestation of the continuation of a posterior infarct into the lateral wall.[1,2,3,5] Unipolar leads from Positions V_7, V_6, and V_5 and from the left arm are much more likely to reveal the lateral portion of the infarct, whereas Lead aV_F yields more reliable evidence of the posterior involvement than Leads II and III.[6,7]

The electrocardiographic diagnosis of infarcts confined largely or exclusively to the lateral wall is more difficult, particularly when only a few leads are available. A pattern characterized by transient RS-T segment depression in Leads I, II, and particularly in IVF, by absence of abnormal Q waves, and by the frequent association of auricular fibrillation was ascribed to lateral infarction by Wood, Wolferth, and Bellet,[8] based upon its demonstration in three patients with postmortem evidence of primary lateral infarction, in one with extensive anterolateral infarction, and in a number of patients with clinical diagnoses of coronary thrombosis. The RS-T segment depression resembled that produced by digitalis, thus necessitating the consideration of cardiac glycosides and transitory ischemia in the differential diagnosis. Thomson and Feil[9] analyzed the available electrocardiograms (consisting of the three standard leads and usually one or two precordial leads) which had been obtained on nineteen patients with postmortem evidence of lateral infarction and found the pattern of Wood and associates in four. In the remainder there were nonspecific abnormalities or changes either suggestive or diagnostic of either anterior or posterior infarction. Shaffer[10] made a similar analysis of the four-lead electrocardiograms of five patients with

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pathologically established lateral infarction and found QRS abnormalities in Lead IV suggestive of anterior infarction in two, evidence suggestive of posterior infarction in two, and changes more in keeping with left ventricular hypertrophy in one. From the foregoing studies, it is evident that the three standard leads supplemented by one or two precordial leads are inadequate for the detection and localization of many infarcts confined to the lateral wall of the left ventricle.

Wilson and associates[2] have pointed out that the six precordial leads which they introduced may be inadequate for the detection of high lateral infarction and have noted QR or QS complexes in the unipolar left arm lead in cases without diagnostic signs in the customary precordial leads. Before interpretation of the significance of a QR or QS complex in Lead aV_L, an effort must be made to determine whether the predominant effect on the recordings in this lead came from the potential variations of the lateral wall of the left ventricle, the posterobasal wall, or the mitral orifice. The method employed in arriving at such a decision has been described in detail[5,11,12] and will be illustrated in a number of the individual case reports in this communication.

In patients with signs suggestive, but not diagnostic of infarction in the customary leads from the left precordium and in patients with abnormal Q-wave patterns in Lead V_L but not in V_1 through V_6, the Wilson group[13,14] has employed supplementary high precordial leads taken at the intersections of vertical lines through the customary left precordial positions with horizontal lines at the level of the sternal terminus of the second, third, and fourth intercostal spaces. They have demonstrated diagnostic QR or QS patterns in certain of the high precordial leads in patients with negative, equivocal, or only slightly suggestive signs of infarction in the customary precordial leads and have interpreted these findings as evidence of a lesion confined to the basal portion of the anterior and/or lateral walls. Abnormal Q-wave patterns localized to, or centered in high axillary leads were attributed to high lateral infarction; those maximal in high leads in the midclavicular and anterior axillary lines were ascribed to a high anterolateral lesion; abnormal Q waves in leads high in the posterior axillary line, coupled with reciprocal exaggeration of the R and T waves in V_1, V_2, and V_3, were attributed to high posterolateral infarction. None of the patients with high precordial leads reported by the Wilson group came to autopsy. However, Hecht[3] has confirmed their observations and conclusions.

In our series of 161 cases of myocardial infarction accurately localized at autopsy, there were 105 (65 per cent) with pathologic evidence of lateral infarction. Separate analyses have been made of a group of fifty-seven patients with large anterior infarcts which extended into the apical one-third or more of the lateral wall[4] and another group of thirty-two with posterior infarcts which continued into the lateral wall.[5] No further reference will be made to these cases, with the following exceptions. In three patients (Cases 151, 152, and 153), autopsy revealed two separate lesions, one of which was a primary lateral infarct involving most of the lateral wall, and the other an anterior infarct which continued into the apical portion of the lateral wall. Electrocardiograms were obtained after each of the two infarcts in all three cases and the findings referable to the antero-

lateral infarct were analyzed previously,[4] whereas those referable to the primary lateral infarct will be considered in this communication. Eight patients (Cases 142, 145, 151, 152, 154, 157, 158, and 159) who had primary lateral infarcts that continued into the posterolateral wall were mentioned in summary of the findings in posterolateral infarction,[5] but will receive detailed consideration herein.

The present study, therefore, has been narrowed to twenty-seven patients with primary lateral infarction which at autopsy was confined to, or located principally in the lateral wall of the left ventricle. Twenty-four of these cases (Cases 138 through 161) will be reported in detail and the remainder (Cases 4, 17, and 60) have been reported in previous communications because of infarction elsewhere in the heart, but will be included in the discussion.

CASE REPORTS

CASE 138.—A 55-year-old man had been in good health until February, 1944, when he began to have typical angina pectoris. On March 9, 1944, he was seized suddenly with an exceptionally severe attack which resulted in syncope. After consciousness returned, the pain was still present and persisted until relieved by morphine. There were classical physical signs of aortic stenosis and laboratory findings compatible with recent myocardial infarction. On March 19 the patient was suddenly seized with extreme dyspnea, accompanied by circulatory collapse, but not by pain. He recovered from this attack, but died suddenly on March 24. No cardiac glycosides were given.

Electrocardiographic Findings.—Electrocardiograms reproduced in Fig. 1,*A* were obtained on March 10, twelve hours after the onset of the thoracic pain and syncope, on March 11, and on March 22, two days before death. The initial phase of the QRS complex was consistently upright in all precordial leads and in the standard limb leads. However, Lead aV_L, which is not reproduced, showed an initial Q wave 1.0 mm. in depth and 20 per cent of the succeeding R wave, followed by a diphasic T wave of low voltage. This finding was consistent with left ventricular hypertrophy and was not considered diagnostic of infarction. The tall R waves in Leads V_5 and V_6 with slurred ascending limbs of 0.04 second duration and the deep S waves of Leads V_1 and V_2 were also strongly suggestive of left ventricular hypertrophy. The R waves of Leads V_5 and V_6 of the second tracing were almost identical in amplitude and configuration with those of the first tracing and the R waves in the same leads of the final electrocardiogram showed a 33 per cent reduction in voltage without alteration in contour. The variations in the QRS pattern in Leads V_3 and V_4 were transitional in type and were attributable to shift in the position of the electrode in reference to the interventricular septum. The most striking change in the serial electrocardiograms took place in the RS-T segment and T wave of the last four precordial leads (V_3 through V_6). In the tracing of March 10 there was an abnormal depression of the RS-T segment in the last three precordial leads, which amounted to 2.0 mm. in V_4 and 1.0 mm. in V_5 and V_6. The following day the RS-T depression had become considerably greater, especially in V_5 and V_6, and the terminal upright portion of the T wave had decreased significantly in amplitude. The Q-T interval was abnormally long. In the final tracing, the RS-T segment was still depressed in Leads V_4, V_5, and V_6, but had changed considerably in contour as a result of the reversal in the direction of the T wave, which had become sharply inverted, not only in these leads, but also in transitional Lead V_3. These changes in the RS-T segment and T wave were comparable to those described by Wood, Wolferth, and Bellet as characteristic of lateral infarction.[8] As mentioned in the history, this patient received no cardiac glycosides or quinidine, so that drug effects could be excluded positively. The differential diagnosis rested between a patchy infarct of the subendocardial aspect of the anterolateral wall of the apex and acute ischemia in the same area. The absence of Q waves was more in keeping with the latter, but did not positively exclude a subendocardial infarct.

Pathologic Findings.—The heart weighed 523 grams as a result of left ventricular hypertrophy secondary to rheumatic aortic stenosis. An organizing infarct of two to three weeks'

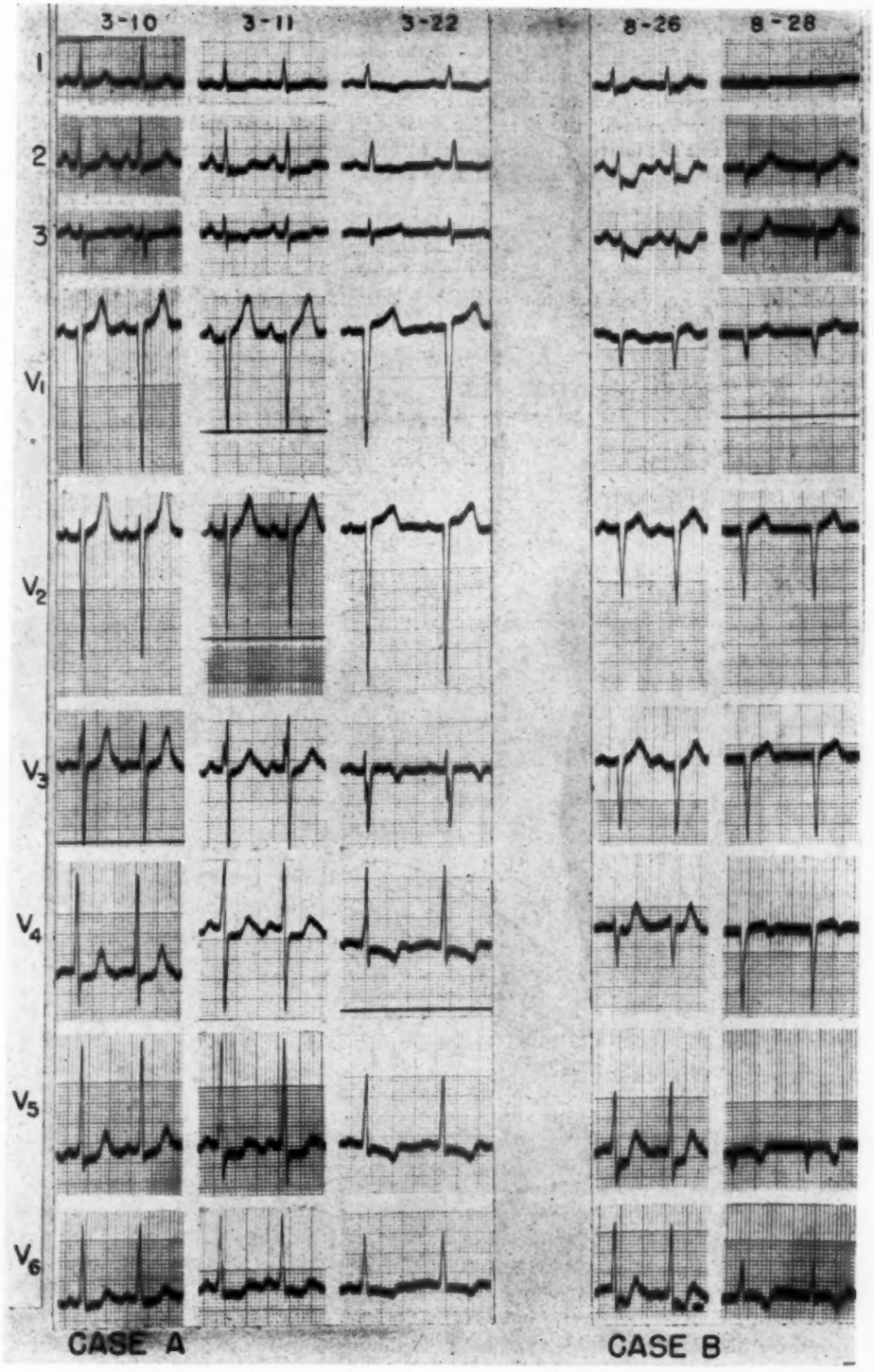

Fig. 1.—Serial electrocardiograms during acute infarction of the anterolateral aspect of the apex. *A*, Case 138; *B*, Case 139.

duration was found in the anterolateral aspect of the left apex, as demarcated by the solid lines of Fig. 2. Upon microscopic examination, the lesion was confined to the subendocardial one-half of the lateral aspect of the apex and was found chiefly in the mid-zone of the anteroapical wall, but extended in fingerlike fashion to the endocardial surface. The subepicardial one-half of the anterolateral wall was not infarcted. There was good correspondence between the serial changes in RS-T segment and T wave and the organizing infarct limited to the subendocardial one-half of the anterolateral wall of the apex. The absence of Q waves may have been due to the relatively small size and patchy character of the subendocardial infarct, but the voltage of the R waves in Leads V_4, V_5, and V_6 was greater than would have been expected in the presence of such a lesion. In view of the autopsy findings, it is possible that the one-third reduction in the voltage of the R wave in Leads V_5 and V_6 of the final tracing may have been significant.

Fig. 2.—Roentgenogram of the injected heart in Case 138.

CASE 139.—A 59-year-old man had been perfectly well up until June, 1944, when he began to notice exertional and paroxysmal nocturnal dyspnea. On August 24 and 25 he had several transient attacks of retrosternal oppression, provoked by exercise and promptly relieved by rest. At noon on August 26 he was seized with severe, crushing retrosternal pain which radiated down the inner aspect of the right arm and led to admission in circulatory collapse three and one-half hours later. The pain was relieved by morphine, but returned early in the morning of the 28th and persisted in spite of further opiates. Death occurred forty-nine hours after admission. No cardiac glycosides were administered prior to or during hospitalization.

Electrocardiographic Findings.—Electrocardiograms obtained at 4:30 P. M. on August 26 and at noon on August 28 are reproduced in Fig. 1,*B*. The first electrocardiogram, taken four and one-half hours after the onset of the pain, was comparable to the original tracing in Case 138.

The initial phase of the QRS complex was upright in all precordial leads except V_1, where there was a QS complex. The QS deflection in V_1 and the minute initial R wave of V_2 and V_3 were within the limits of normal variation. The electrode at precordial Position 4 was near the transitional zone, whereas that at Positions 5 and 6 reflected the potential variations of the anterolateral aspect of the left ventricle. The striking feature of the precordial leads was the 2.0 mm. depression of the RS-T segment in Leads V_5 and V_6. This depression could not have been reciprocal to a transmural posterior infarct, since Leads aV_F, II, and III showed an RS complex with a 2.0 mm. RS-T depression comparable to that in V_5 and V_6. Digitalis effects were excluded positively from the history. The differential diagnosis lay between an acute ischemia of the subendocardial portion of the anterolateral and posterior aspects of the apex and a patchy subendocardial infarct in the same location. The absence of Q waves was in favor of the former, but did not exclude the latter. Lead aV_L showed a normal R wave, an isoelectric RS-T junction, and upright T wave, and was apparently reflecting the potential variations of a portion of the lateral wall of the left ventricle basal to the lesion. A study of the tracing of August 28 revealed striking changes in the QRS complex of the last three precordial leads, particularly of V_5. The formerly tall R wave in this lead was reduced to 1.0 mm. and was preceded by an abnormal Q wave 5.0 to 6.0 mm. deep. The formerly tall, upright T wave had become sharply inverted and the RS-T segment had become isoelectric. The changes in the QRS deflection in Lead V_5 were pathognomonic of incomplete transmural infarction of the anterolateral wall of the left apex, and the changes in the RS-T compex and T wave in this lead signified that the lesion which formerly had been limited to the subendocardial portion of the wall had extended to involve the subepicardial layer of muscle. In Lead V_4 the initial R wave almost disappeared, the RS-T junction became isoelectric, and the RS-T segment and T wave reversed in direction. In view of the findings in Lead V_5, those in V_4 were interpreted as indicating that the original subendocardial lesion had extended in patchy fashion through the anteroseptal portion of the left apex. The initial upright deflection in Lead V_6 persisted, but was reduced to 50 per cent of its former amplitude. The RS-T junction in this lead became isoelectric and the T wave exhibited sharp cove-like inversion. These changes were due most likely to extension of the lesion in patchy fashion through the lateral aspect of the apex, but might have been the result of infarction confined to the subepicardial one-half of this region. Comparable changes occurred in the R wave and T wave of Lead I. The formerly depressed RS-T segments in Leads II and III became isoelectric and the T waves became tall, upright, and reciprocal in contour to those of V_5 and V_6. Unfortunately, Lead aV_F was not obtained on August 28. The changes in standard Leads II and III were due most likely to a disappearance of the ischemia of the subendocardial portion of the posterior wall together with the development of reciprocal effects from the acute infarct of the anterolateral aspect of the apex.

Pathologic Findings.—The heart weighed 500 grams and revealed an acute infarct of the anterolateral wall of the apex, almost identical in position with that in Case 138 (Fig. 2), except for the absence of the knoblike extension toward the posterior wall. On microscopic examination, the infarct was estimated to be one to two days old. It involved principally the subendocardial one-half of the wall, but exhibited fingerlike projections to the epicardium together with a complicating pericarditis. The findings at autopsy thus confirmed the position and character of the infarct, as predicted from the QRS-T pattern in the tracing of August 28. The status of the lesion at the time of the first electrocardiogram, made four and one-half hours after the onset of symptoms and forty-eight hours before death, was left unsettled. On the basis of the histologic findings, it was impossible to reach a positive conclusion as to whether the lesion found at autopsy had commenced before or after the time of the first electrocardiogram. Judging from the profound circulatory collapse, it seemed likely that the subendocardial lesion found at autopsy had begun prior to admission. If so, the marked RS-T segment depression in Leads V_4 through V_6 constituted the earliest manifestation of a developing subendocardial infarct, and the concurrent registration of a normal initial R wave in these leads was best explained by the assumption that the degenerative changes were not sufficiently advanced to have prevented the response to the activating impulse. However, it is conceivable that the lesion at the first electrocardiogram consisted merely of subendocardial ischemia and that the histochemical changes of anterolateral infarction developed subsequently. Since the posterior wall of the apex was negative histologically, the

transient RS-T segment depression in Leads II and III was apparently the result of a transient ischemia of the posterior aspect of the apex.

CASE 140.—A 65-year-old man was brought to the hospital four hours after the sudden onset of constrictive retrosternal pain which radiated down the left arm and was accompanied by severe dyspnea. Death occurred thirty-one hours after admission. No cardiac glycosides were given.

Electrocardiographic Findings.—An electrocardiogram was obtained twelve hours after admission, but is not reproduced because of its resemblance to the last tracing (March 22) in Case 138 (Fig. 1,*A*). There was no significant difference in the QRS pattern in the first four precordial leads of the two patients. Comparison of Leads V_5 and V_6 of this patient with those of the electrocardiogram of March 22 (Fig. 1,*A*) revealed that the R wave was only about two-thirds as tall and was preceded by a minute Q wave, whereas the depressed RS-T segment and inverted T wave were similar in contour. The QRS-T pattern in the standard leads was similar in the two cases, except that the R wave of Lead I in this case was coarsely notched and only one-half as tall. In Lead aV_L in this case there was coarse notching of the upstroke of the R wave, an isoelectric RS-T junction, and a sharply inverted T wave. The findings in Leads V_5, V_6, and aV_L might have been due to ischemia or patchy infarction of the subendocardial layer of the anterolateral wall or merely to uncomplicated left ventricular hypertrophy. For a positive differentiation, further tracings would have been required, but were not obtained because of the early death of the patient.

Pathologic Findings.—The heart weighed 460 grams and revealed a recent small infarct in the anterolateral wall of the apex, comparable in size and position to that in Case 138 (Fig.2), except for the lack of the knoblike projection toward the posterior wall. This infarct was mainly in the mid-zone at the apex and became subendocardial near its upper border in the anterolateral wall. The patchy character and relatively small size of the infarct probably accounted for the lack of abnormal Q waves. The RS-T depression and inverted T waves of Leads V_5 and V_6 could be correlated with involvement of the subendocardial and mid-zones and sparing of the subepicardial layer.

CASE 141.—A 46-year-old man had noticed gradually increasing exertional dyspnea since 1938 and paroxysmal nocturnal dyspnea since 1941. He gave no history of chest pain until Nov. 23, 1943, when he had two brief attacks of mild retrosternal constriction. On Dec. 10, 1943, he was seized with a vise-like retrosternal pain, which lasted until morphine was given on hospitalization five hours later. Because of refractory congestive failure, digitalis was started on Jan. 24, 1944, and given in a dose of 0.2 Gm. daily until February 5. Severe retrosternal pain recurred on January 30. A pericardial friction rub was heard at the apex on February 5 and persisted until his death on February 12.

Electrocardiographic Findings.—Electrocardiograms selected from a series during his two months' hospital stay are reproduced in Fig. 3. The initial tracing, taken on Dec. 11, twenty hours after the onset of the pain, revealed signs typical of a large anterolateral infarction, namely, a distinct initial R wave in V_1, a questionable initial R wave in V_2, a QS complex, elevated RS-T junction and cove-shaped inversion of the T wave in V_3, and an abnormal QR complex with elevated RS-T junction and typical "coronary" T wave in Leads V_4, V_5, V_6, and aV_L. The deep Q wave of Lead aV_L was practically obliterated from Lead I because of the concurrent initial negativity of the right arm. In succeeding tracings an initial R wave, deep S wave, slightly elevated RS-T junction, and normal upright T wave were consistently found in Leads V_2 and V_3 and a QS complex appeared in V_4. The RS-T segments and T waves in Leads V_4, V_5, and V_6 showed the usual evolution until January 28, when there was a recurrence of the upward displacement of the RS-T junction. The RS-T segment elevation became more marked on February 4, which was the first tracing taken after the second attack of severe retrosternal pain. These changes indicated further injury to the subepicardial aspect of the anterolateral wall of the left ventricle and could have been due to reinfarction or to intercurrent pericarditis.

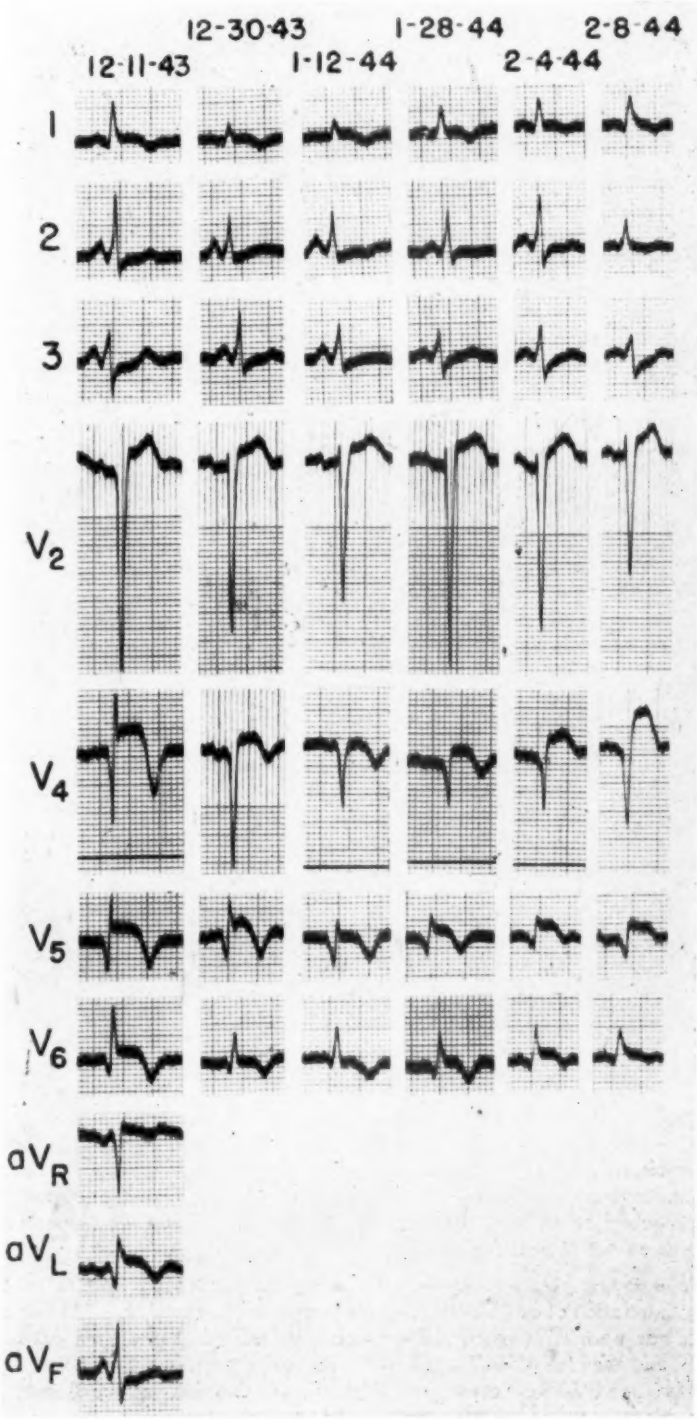

Fig. 3.—Serial electrocardiograms in Case 141.

Pathologic Findings.—The heart weighed 501 grams and exhibited an organizing infarct, occupying most of the apical two-thirds of the lateral aspect of the left ventricle, as demarcated by the solid line of Fig. 4. In its thinnest portion the lateral wall was 3.0 mm. in thickness. Microscopic examination showed an organizing infarct, extending patchily from endocardium to epicardium with a recent reinfarction one to two weeks old affecting the portions of the subepicardial muscle which had been spared in the first attack. Although this infarct did not reach the junction of the anterior wall and septum, it apparently extended far enough into the anterior wall to produce classical findings in Lead V_4. The QR patterns in Leads V_5 and V_6 corresponded quite well with the involvement of the anterolateral and lateral walls of the left ventricle, and those in V_1, V_2, and V_3 of all tracings made subsequent to December 11 corresponded with the sparing of the anteroseptal wall of the left ventricle. The transient abnormality in the initial phase of the QRS complex noted only in the first tracing may have been due to early injury to the anteroseptal wall with subsequent spontaneous reversal. The increased RS-T segment elevation in the last two tracings reflected injury to the subepicardial muscle consequent upon the reinfarction found at autopsy.

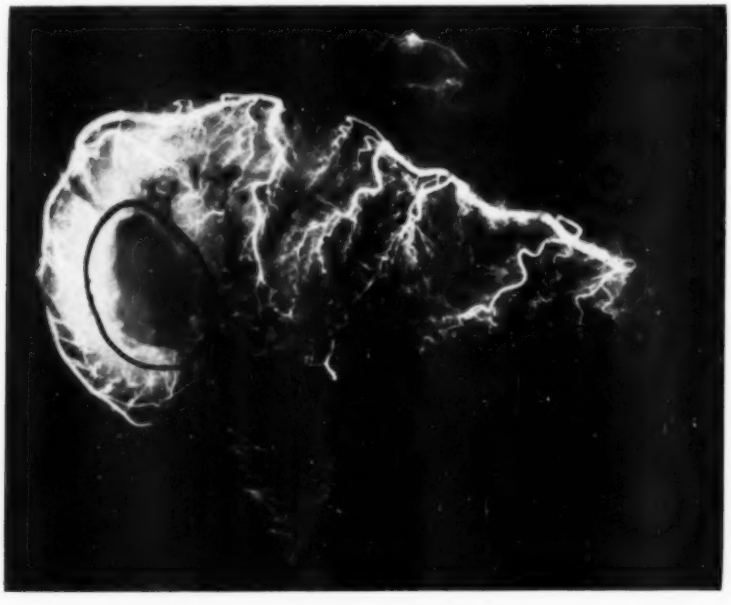

Fig. 4.—Roentgenogram of the injected heart in Case 141, showing large lateral infarct.

CASE 142.—A 46-year-old man was admitted to the hospital with a history of dyspnea, cough, hemoptysis, right-sided pleural pain, and fever of two weeks' duration. No definite history of myocardial infarction could be elicited. Physical examination revealed congestive failure complicated by bronchopneumonia. Although the pneumonia resolved, decompensation persisted, ending in death on the fifteenth hospital day.

Electrocardiographic Findings.—An electrocardiogram obtained six hours after admission and before the administration of cardiac glycosides is reproduced in Fig. 5,*A*. The initial phase of the QRS complex was upright in the first four precordial leads and measured 4.0 mm. in V_1 and 5.0 mm. in V_2, and then fell off to 3.0 mm. in V_3 and to 2.0 mm. in V_4. The abnormal QR complexes in Leads V_5 and V_6 were considered diagnostic of infarction and the T waves in these leads suggested an old, rather than a recent, lesion. In Lead aV_L there was a relatively deep Q wave and a small late R wave suggestive of infarction. Because of the inversion of the P wave in Lead

aV_L, it was necessary to consider transmission of potential variations of the left atrium to the arm as an alternative explanation for the QR pattern in aV_L.[11,12] However, in subsequent tracings taken in the sitting position, an abnormal QR pattern was recorded in aV_L in association with an upright P wave. This was interpreted as evidence that the findings in Lead aV_L were due to

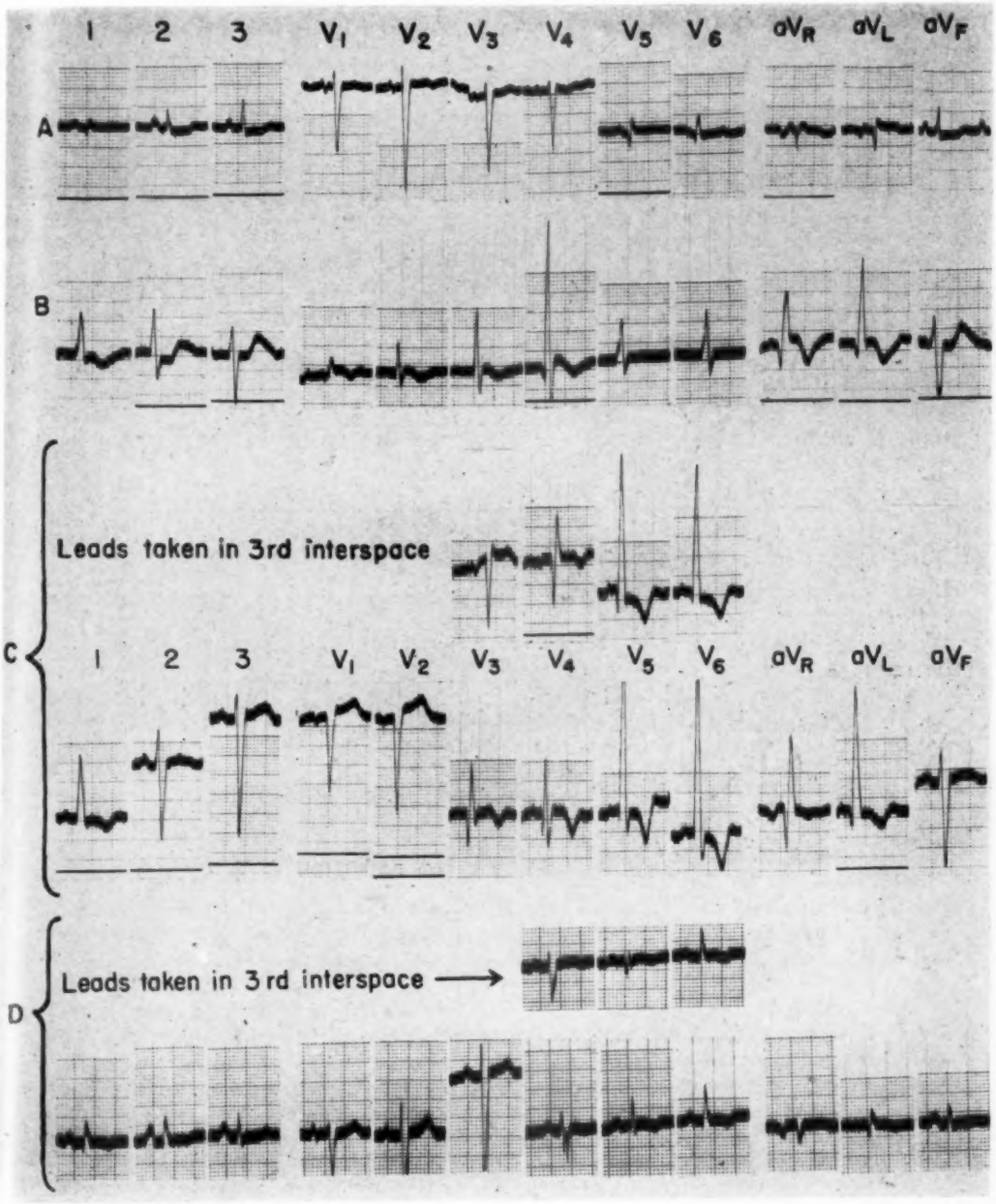

Fig. 5.—Electrocardiograms in lateral infarction. *A*, Case 142; *B*, Case 143; *C*, Case 144; *D*, Case 145.

lateral infarction. The abnormal QR complex of aV_L tended to carry over into Lead I, but the Q wave was greatly reduced in amplitude because of the concurrent negativity of the right arm. Thus, the QR pattern in Lead I was not as abnormal as that in aV_L. The elevation of the RS-T junction and monophasic upright T wave in aV_L of the first tracing, together with the reciprocal depression of the RS-T segment in aV_F, was suggestive of recent lateral infarction, and the subsequent return of the RS-T junction to the isoelectric line constituted further supportive evidence. On the other hand, the T wave in aV_L, V_5, V_6, and Lead I failed to undergo the cove-like inversion typical of organizing infarct. Thus, the age of the lateral infarct remained in doubt.

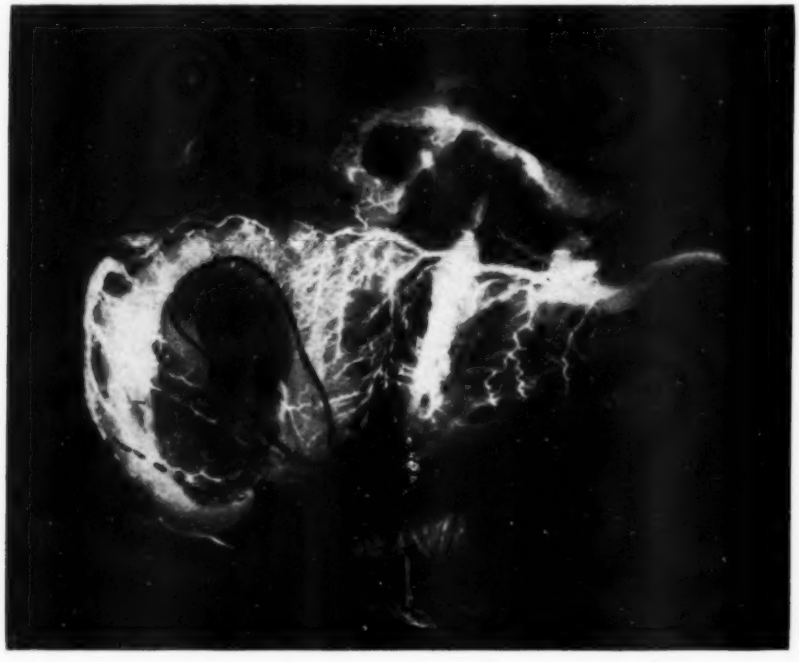

Fig. 6.—Roentgenogram of the injected heart in Case 142, showing large, recent lateral infarct in solid outline and old, healed anteroseptal infarct in broken lines.

Pathologic Findings.—The heart weighed 388 grams and revealed an organizing lateral infarct, demarcated by the solid lines of Fig. 6, and an old, completely healed infarct, which involved the apical one-half of the anteroseptal wall and extended slightly into the lateral wall at the tip of the apex, as indicated by the broken lines of Fig. 6. There was moderate right ventricular dilatation, apparently due to the combination of the left heart failure and pneumonia. After a review of the electrocardiograms in the light of the autopsy findings, it was concluded that the right ventricular dilatation was responsible for the RS pattern in the first four precordial leads and that the transitional zone was between Positions 4 and 5. This right ventricular dilatation could have produced sufficient clockwise rotation of the heart to cause transmission of the potential variations of the anteroseptal aspect of the left ventricle to the axilla instead of to Positions 3 and 4. The old healed anteroseptal infarct was considered the more likely cause of the abnormal QR pattern in Leads V_5 and V_6 than the recent lateral infarct because of the absence of the characteristic serial changes in the RS-T segment and T wave from these leads The fact that the RS-T segment was originally elevated in Lead aV_L and reciprocally depressed in aV_F and subsequently isoelectric in both leads suggested that the pattern in aV_L was produced by the recent high lateral infarction. Although this infarct extended into the posterolateral wall near the apex, characteristic changes were not produced in Lead aV_F.

CASE 143.—A 63-year-old woman was brought to the hospital in coma complicated by profound circulatory collapse. No further history was obtainable. Death occurred one hour after admission. No cardiac glycosides were given.

Electrocardiographic Findings.—An electrocardiogram obtained one-half hour after admission is reproduced in Fig. 5,*B*. Interference dissociation was present with an atrial rate of 70 and a regular ventricular rate of 90 per minute. The ventricular complexes were uniform in any given lead and thus arose from a single focus. The following interpretation was based on the supposition of a nodal, rather than idoventricular, pacemaker. The duration of the QRS complex was 0.12 second and abnormal slurring or notching was present in every lead except V_3. An initial Q wave was recorded in Leads V_1, V_2, and V_4, but was absent from most cycles of Lead V_3, probably because the first portion of the QRS complex was isoelectric in this lead. This assumption was supported by the fact that the measurable QRS duration in V_3 was only 0.08 second, as compared with 0.12 second in leads to the right and left. The Q wave of Lead V_1 was followed by a notched upstroke, late intrinsicoid deflection, elevated RS-T junction, and coved inversion of the T wave. Lead aV_R also displayed a Q wave, prominent late R wave, elevated RS-T junction, and deeply inverted T wave. The findings in Leads V_1 and aV_R were subject to two widely divergent explanations: (1) anteroseptal infarction, involving enough of the septum to produce the pattern of right bundle branch block in Leads V_1 and aV_R and continuing sufficiently into the subendocardial portion of the anterior wall to account for the Q wave in Lead V_4; (2) rotation of the heart, so that the potential variations of the posterobasal aspect of the left ventricle were transmitted to the right arm and carried through to the right anterior chest wall to produce the QR pattern in V_1. It was difficult to reconcile the second alternative with the fact that the transitional zone was apparently near the midline anteriorly and the potential variations of the anterior and lateral walls of the left ventricle were referred to precordial Positions 2 to 6, inclusive. This would have meant that the potential variations of some portion of the epicardial surface of the left ventricle would have been referred around the entire circumference of the chest, which was anatomically implausible. Hence, the first alternative was favored. The pattern in Leads V_2 and V_3 was subject to slight cyclic variation, a minute initial Q wave usually being present in V_2 and absent from V_3, but in a minority of cycles the Q wave was absent from V_2 and present in V_3. A Q wave was consistently present in Lead V_4 and varied from 2.0 to 4.0 mm. in depth and from 5 to 10 per cent of the amplitude of the succeeding R wave. Despite the low Q/R ratio, the Q wave was considered abnormal because of its coarse slurring and because of the 0.04 second interval from its onset to nadir. This, together with the RS-T elevation and T-wave inversion, pointed to a recent patchy infarct. Leads V_5 and V_6 showed an initial upstroke that was abnormally slurred and prolonged. The pattern in Lead aV_L, on the other hand, resembled that of V_4 and, along with the findings in the first four precordial leads, suggested infarction of the subendocardial layer of the basal portion of the anterolateral wall. The Q wave of aV_L was oblitereated in Lead I because of the simultaneous greater negativity of the right arm. Death occurred before additional high precordial leads could be taken.

Pathologic Findings.—The heart weighed 341 grams and exhibited a calcareous aortic stenosis. By means of multiple microscopic blocks encircling the ventricle, an acute subendocardial infarct was found localized to the areas demarcated by the solid line in Fig. 7. This infarct involved the lateral wall at the base and extended diagonally forward into the anterior wall near the apex, but spared the septum and right ventricle. It apparently had occurred as a terminal event secondary to the peripheral circulator collapse consequent upon cerebral hemorrhage, which was the primary cause of death. The involvement of the anterior wall near the apex was probably responsible for the pattern in V_4, and the high lateral part of the infarct may have accounted for the findings in Lead aV_L. In view of the counterclockwise cardiac rotation and displacement of the transitional zone to the right, the infarction of the subendocardial layer of the anterolateral wall in the basal segment may have been responsible for the QR pattern in Leads V_1 and V_2. Since the electrocardiogram was obtained shortly before death, the bizarre findings may have reflected terminal functional changes independent of the demonstrated anatomical lesions.

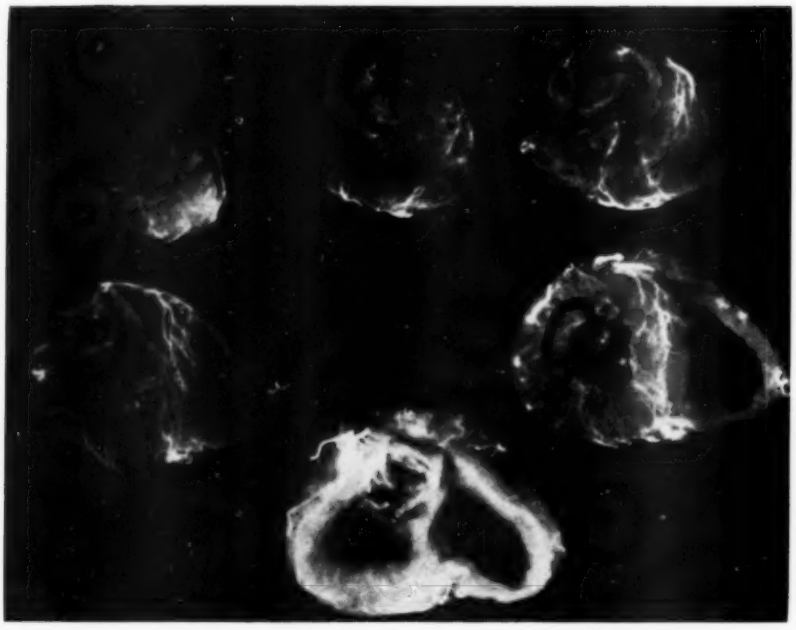

Fig. 7.—Roentgenogram of the injected heart in Case 143.

CASE 144.—A 72-year-old man was admitted to the hospital in coma and died without regaining consciousness. No history was obtainable. No cardiac glycosides were given.

Electrocardiographic Findings.—An electrocardiogram obtained on the first hospital day is reproduced in Fig. 5,*C*. In Leads V_6, V_7, and V_8 there was an exceptionally tall initial R wave, slightly delayed onset of intrinsicoid deflection, depression of the RS-T junction, and inversion of the T wave indicative of left ventricular hypertrophy. The QS complex in Lead V_1 and the minute R and deep S waves in V_2 were compatible with left ventricular hypertrophy. A triphasic QRS complex was recorded in the next three precordial leads. In Lead V_3 this was characterized by a Q wave 7.0 mm. in depth and 60 per cent of the succeeding R wave; in V_4 there was a Q wave 5.0 mm. in depth and 35 per cent of the subsequent upright deflection; whereas in V_5 there was a relatively small Q wave, which was only 7 per cent of the extremely tall R wave. The findings in Lead V_5, like those in V_6, were compatible with left ventricular hypertrophy. On the other hand, the findings in V_3 and V_4 were indicative of infarction and were attributed to a lesion involving the subendocardial portion of the anteroseptal wall of the left ventricle. Because of the slightly elevated, dome-shaped RS-T segment and sharply inverted T wave in these leads the infarct was considered to be of recent origin. For further localizing evidence, additional leads were obtained from points at the intersections of a horizontal line bisecting the junction of the third intercostal space and sternum with vertical lines through precordial Positions 3 through 6. A much deeper Q wave and smaller R wave were recorded in the high leads above Positions 3 and 4. This was interpreted as evidence that the major portion of the infarct was located high in the anteroseptal wall of the left ventricle. In the high anterior axillary lead, there was a 6.0 mm. Q wave which was about 15 per cent of the amplitude of the tall R wave. This was compatible with, but not diagnostic of, a thin subendocardial infarct, occupying but a small fraction of the greatly hypertrophied lateral wall. In both the high midaxillary lead and in aV_L there was a relatively small Q wave 2.0 to 4.0 mm. in depth followed by an exceptionally tall R wave, delayed intrinsicoid deflection, depressed RS-T junction, and inverted T wave, which were more in keeping with uncomplicated left ventricular hypertrophy than with infarction.

The findings in Lead aV_L coupled with those in aV_F indicated that the heart was in horizontal position. The tall R wave in aV_R was probably due to transmission of the potential variations of the posterobasal aspect of the left ventricle to the right arm.

Pathologic Findings.—Death was due to a cerebral hemorrhage which had ruptured into the fourth ventricle. The heart weighed 472 grams and showed considerable concentric left ventricular hypertrophy. By means of multiple microscopic blocks, a small organizing infarct was found localized to the subendocardial portion of the lateral wall of the left ventricle at the base, as outlined in Fig. 8. There was no evidence of infarction of the anteroseptal wall of the left ventricle. In view of the horizontal position revealed by Leads aV_L and aV_F and the displacement of the transitional zone to the right between precordial Positions 2 and 3, it is probable that sufficient counterclockwise rotation was present to bring the basal portion of the lateral wall of the left ventricle into a position which facilitated transmission of its potential variations to points on the precordium. In this manner the electrocardiographic patterns of infarction found in leads taken at the parasternal and midclavicular lines might be correlated with the pathologic demonstration of an infarct limited to the lateral aspect of the basal portion of the left ventricle.

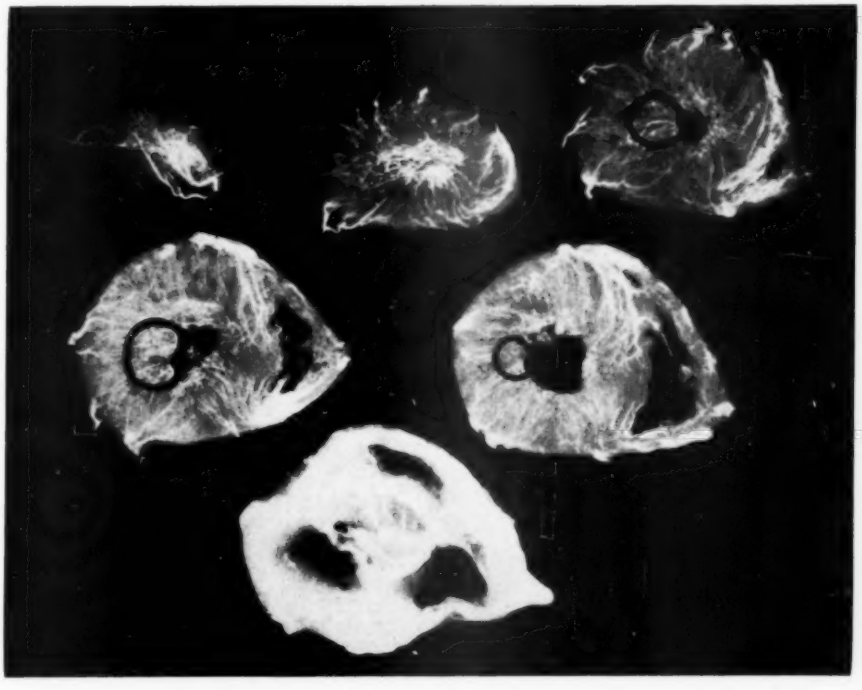

Fig. 8.—Roentgenogram of the injected heart in Case 144, outlining the position of a subendocardial lateral infarct.

CASE 145.—A 54-year-old man gave a two-year history of transient retrosternal constriction and dyspnea, precipitated by exercise and promptly relieved by rest, but recalled no attacks of prolonged pain. He was admitted to the hospital in congestive heart failure with auricular tachycardia and gradually became compensated after the spontaneous return of sinus rhythm. On the twenty-eighth day auricular tachycardia recurred, resulting in sudden left ventricular failure and death.

Electrocardiographic Findings.—An electrocardiogram obtained before the administration of digitalis is reproduced in Fig. 5,*D*. The first four precordial leads showed an RS complex

and the last two showed a minute insignificant Q wave preceding a normal upright deflection. The R wave increased from 2.0 mm. in Lead V_1 to 8.0 mm. in V_2, remained constant in V_3, decreased to 4.0 mm. in V_4, and progressively increased in V_5 and V_6. The notched, equiphasic RS deflection in Lead V_4 suggested that the electrode lay over the septum and that the localized reduction in the R wave might have been a transitional effect. The RS-T segments and T waves of V_5 and V_6 were somewhat suggestive of an ischemic zone beyond the boundary of an infarct, but were compatible with uncomplicated left ventricular hypertrophy. The equiphasic QR deflection and inverted T wave in Lead aV_L were more distinctive than the findings in the precordial leads, but could not be properly interpreted until the portion of the heart which had the predominant effect on the potential variations of the left arm was determined. The findings in Lead aV_L were not transmitted from the posterobasal wall of the left ventricle because of the prominent R wave in Lead aV_F, which indicated that the potential variations of the posterior wall

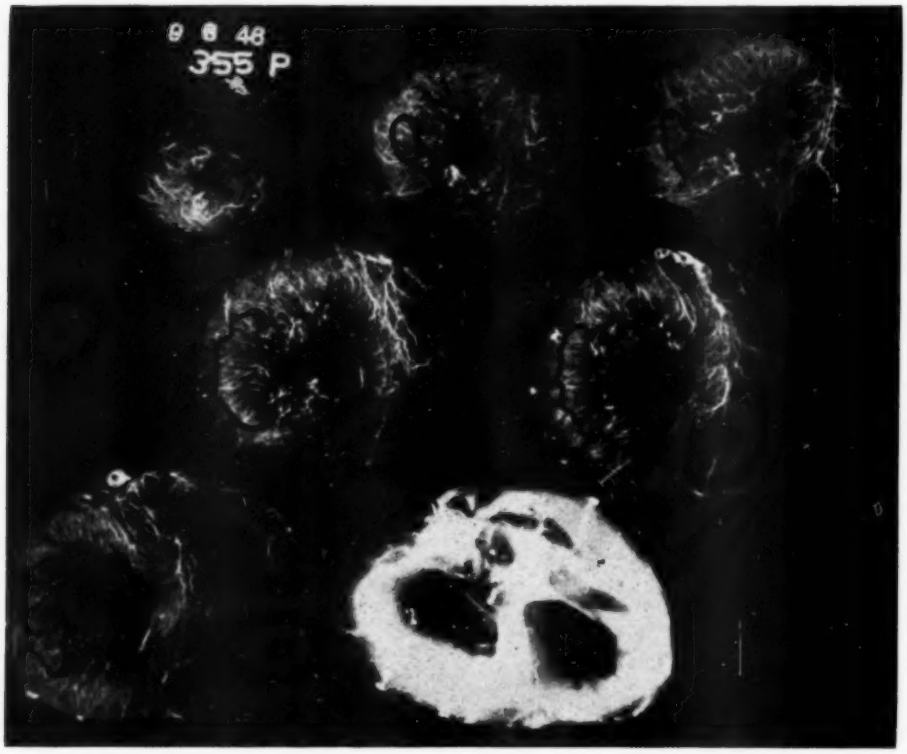

Fig. 9.—Roentgenogram of the injected heart in Case 145.

of the left ventricle were directed downward. The findings in aV_L were probably not due to cavity potentials transmitted through the mitral orifice to the left arm because the cardiac position which facilitates such a pathway leads to the registration of an inverted P wave in Lead aV_L. It was therefore concluded that the heart was in intermediate position and that the potential variations of the epicardial surface of the lateral wall of the left ventricle had the predominant effect upon the QRS-T pattern in Lead aV_L. The QR complex in Lead aV_L was considered strongly suggestive of lateral infarction, but could not be regarded as pathognomonic because of the low voltage of the QRS complex and the Q-wave duration below 0.03 second. The findings in aV_L were carried over into Lead I, but the Q wave was reduced in depth in Lead I because of the concurrent initial negativity of the right arm. Four other electrocardiograms were taken

during the hospital course and showed no significant changes in the QRS complexes of either the precordial or limb leads and no changes in the T waves other than those attributable to digitalis. For this reason, the lesion was considered to be old and healed. For further localizing evidence, additional leads were obtained from points at the intersections of a horizontal line at the level of the junction of the third intercostal space and sternum with vertical lines through precordial Positions 4, 5, and 6. The tracing taken at the level of the third intercostal space in the midclavicular line closely resembled Lead V_4, and that taken high in the midaxillary line was almost identical with Lead V_6. However, the record from the anterior axillary line at the level of the third intercostal space was characterized by an abnormal QR complex and dome-shaped RS-T segment. This finding, when compared with the customary Lead V_5 and with other records taken at the same horizontal level, was diagnostic of a localized high lateral infarction.

Pathologic Findings.—The heart weighed 749 grams because of left ventricular hypertrophy. A patchy healed infarct which involved the subendocardial one-half of the lateral wall, as outlined in Fig. 9, was found grossly and confirmed microscopically. The extension into the posterolateral wall of the apex was not evident in Lead aV_F, but might have constituted an indirect factor in the relatively high R waves in Leads V_2 and V_3. The infarction of the basilar portion of the lateral wall adequately accounted for the QR pattern in aV_L and in the lead high in the anterior axillary line, whereas the absence of infarction of the anterolateral aspect of the apex could explain the lack of a diagnostic pattern in Leads V_4, V_5, and V_6. This case illustrates well the value of supplementary high precordial leads in the diagnosis of infarcts situated high in the lateral wall of the left ventricle.

CASE 146.—A 72-year-old man had had classical angina pectoris for two years. On June 1, 1945, he was seized with a much more severe attack of retrosternal constriction followed by syncope. He was brought to the hospital in shock one hour later and remained in profound circulatory collapse until his death thirty-nine hours after admission.

Electrocardiographic Findings.—Electrocardiograms reproduced in Fig. 10 were obtained on June 1, two hours after the onset of the pain and before the administration of cardiac glycosides, and on June 2, twenty-two and one-half hours later, after the administration of 1.6 mg. of Cedilanid. In the record of June 1, there was a marked sinus bradycardia (36 per minute) with occasional escaped nodal beats. The initial phase of the QRS complex was upright and normal in contour in all precordial leads. The striking feature of the first five precordial leads was the marked depression of the RS-T junction, the exceptionally broad U-shaped T wave, which caused moderate prolongation of the Q-T interval. The administration of quinidine and allied drugs could be excluded positively. Two possible causes for the RS-T depression remained for serious consideration: (1) a reciprocal manifestation of a recent posterolateral infarct; and (2) a direct result of acute ischemia or early infarction of the subendocardial portion of the anterolateral wall of the left ventricle and the adjoining left side of the septum. The slight elevation of the RS-T junction in Leads V_6 and aV_F raised the question of recent posterolateral infarction. The absence of a Q wave from these leads and the contour of the RS-T segment and T wave were against posterolateral infarction, but did not exclude it, because of the short interval between the onset of symptoms and the recording of the electrocardiogram. Nevertheless, a diagnosis of acute ischemia or very early infarction of the subendocardial portion of the anterolateral wall of the left ventricle and left side of the septum was favored in the ante-mortem interpretation because the downward displacement of the RS-T segment in the first five precordial leads greatly exceeded the upward displacement in V_6 and aV_F. Lead aV_L showed an M-shaped QRS complex of very low voltage and an inverted T wave, which were probably transmitted from the transitional zone as a result of semivertical position of the heart. In the next tracing there was no significant change in the QRS pattern in the standard leads or in aV_R, aV_L, V_1, and V_2. The initial phase of the QRS complex was still upright in the four remaining precordial leads, but was reduced to approximately one-third of its former voltage. The marked decrease in the amplitude of the R wave in these leads was suggestive of patchy infarction of the anterolateral wall of the left ventricle. Close scrutiny of Lead aV_F disclosed the appearance of a minute Q wave 0.5 mm. in depth without significant change in the upright deflection. Although this Q wave was too small to be of diagnostic significance, the parallelism of the T-wave evolution to that of Lead V_6 suggested that the lesion

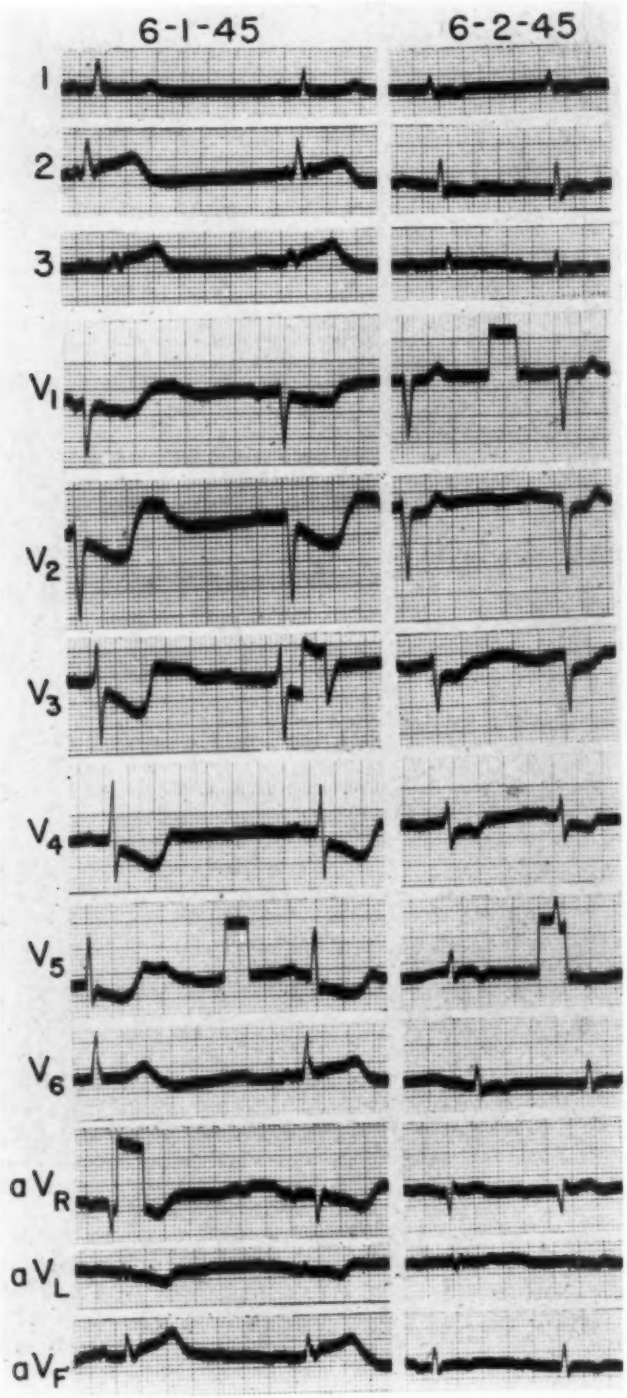

Fig. 10. Serial electrocardiograms in Case 146.

responsible for the changes in V_6 was so placed as to influence the potential variations of the left leg as well. However, the changes in the RS-T segment and T wave were difficult to evaluate because of the administration of Cedilanid during the interim between the two tracings. The marked shortening in the Q-T interval to normal could be ascribed to the combined effects of the acceleration in rate and the Cedilanid. On the other hand, the domelike contour of the RS-T segment in Leads V_5, V_6, and aV_F is an unusual manifestation of cardiac glycosides, but may be produced by toxic doses. The combination of the reduction in voltage in the R wave and the appearance of a domelike RS-T segment and inversion of the terminal portion of the T wave of V_5 and V_6 was more likely a manifestation of a patchy infarct with associated epicarditis involving the lateral wall of the left ventricle and extending sufficiently into the posterior aspect to account for the pattern in Lead aV_F. Although a considerable change had occurred in the contour of the RS-T segment and T wave in Leads V_1 through V_4, the magnitude of the depression of the RS-T junction in V_2 through V_4 was almost as great as in the first tracing. The question still arose as to whether this depression was a reciprocal manifestation of a recent posterolateral infarction or a direct result of acute ischemia or early patchy infarction of the subendocardial portion of the anteroseptal wall.

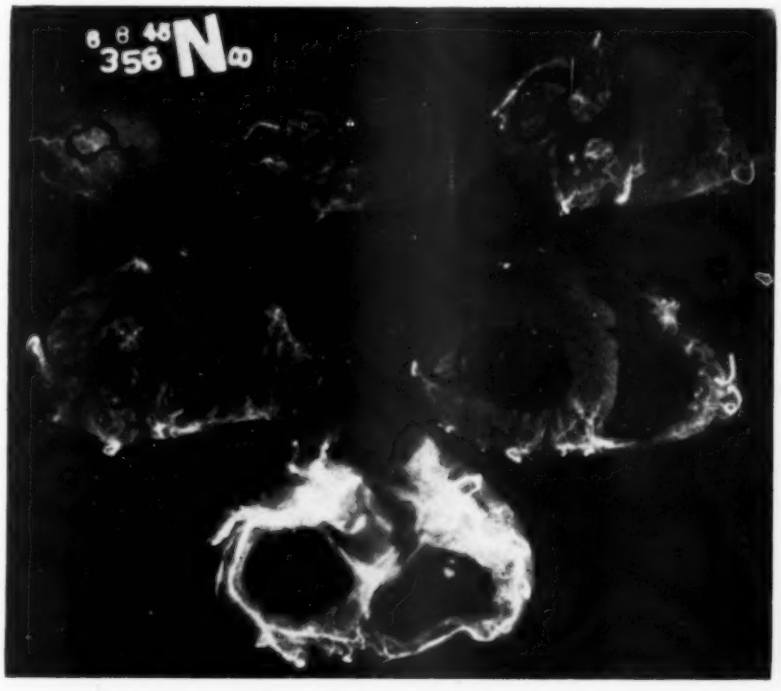

Fig. 11.—Roentgenogram of the injected heart in Case 146 with lateral infarct outlined in black and the anteroseptal ischemia demarcated by its lack of injection.

Pathologic Findings.—The heart weighed 560 grams and showed moderate left ventricular hypertrophy. The striking feature of the roentgenogram (Fig. 11) was the lack of injection of the entire anterior wall of the left ventricle and septum, which was due to an occlusion of the anterior descending coronary artery near its origin. Nevertheless, several microscopic sections through this avascular area showed no evidence of infarction. On the other hand, definite microscopic signs of recent infarction were found in the lateral wall of the left ventricle, as demarcated by the solid lines of Fig. 11. This lateral infarct was transmural at the base and subendocardial at the apex and was probably responsible for the abnormal reduction in the amplitude of the R wave in

Leads V_5 and V_6 and for the T-wave changes in these leads. Since the heart was in semivertical position, sufficient clockwise rotation may have been present to permit transmission of the potential variations of the infarcted area to the left leg, thereby causing the T-wave evolution in aV_F. In view of the occlusion of the anterior descending coronary artery, it is probable that there was sufficient ischemia of the subendocardial portion of the anterior wall of the left ventricle and septum to have caused the downward displacement of the RS-T segment in the first four precordial leads. This seems a more logical explanation of the marked displacement than a reciprocal manifestation of the lateral infarct.

CASE 147.—A 65-year-old man gave a history of intermittent attacks of retrosternal pain, radiating down both arms, accompanied by dyspnea, precipitated by exertion, and relieved by rest. However, he remained at work until one week before hospital admission, when he was suddenly seized with a much more severe epigastric pain accompanied by marked prostration. He entered the hospital because of persistence of the pain and increasing dyspnea. Death occurred fifty-four hours later. No cardiac glycosides were given.

Electrocardiographic Findings.—An electrocardiogram obtained thirty-five hours after admission is reproduced in Fig. 12,*A*. In Lead aV_L there was a QR complex, consisting of a Q wave 3.0 mm. deep, an R wave 4.0 mm. tall, an elevated RS-T segment, and a sharply inverted T wave. Although these findings strongly suggested lateral infarction, it was necessary to consider the possibility that they might have been due to transmission of the potential variations of the normal left atrium to the left arm. The P wave in aV_L was isoelectric and thus of no aid in the differential diagnosis. Considerable indirect help was obtained from the QRS pattern in Lead aV_R. If the QR complex in aV_L had been due to vertical position of the heart, a comparable QR or a QS wave should have been registered in Lead aV_R. The presence of a prominent initial R wave in Lead aV_R was against vertical position, but was compatible with the presence of lateral infarction. The small triphasic QRS complex of Lead aV_F was considered transitional and due to transmission of the potential variations of the posterior aspect of the interventricular septum to the left leg. An abnormal Q wave was registered in Lead I because of the initial positivity of the right arm as well as the negativity of the left arm. A small Q wave was found in Lead II because of the initial positivity of the right arm. Thus, the standard leads were in accord with the diagnosis of lateral infarction. Signs of the lateral infarct evident in Lead aV_L and in the standard leads were not found in V_5 and V_6. An RS deflection and an upright T wave were registered in Leads V_2 through V_6 and were of comparable contour, merely exhibiting a gradual increase in the ratio of the R wave to the S wave as the electrode was moved to the left. The findings in Leads V_2 through V_6 were considered transitional in origin as a result of parallelism between the long axis of the interventricular septum and the pathway of the electrode from Position 2 to Position 6. Thus, Leads V_2 through V_4 were dominated apparently by the potential variations of an area on the anterior surface just to the right of the interventricular septum, while V_5 and V_6 were probably dominated by potential variations of a point on the anterolateral surface just to the left of the interventricular septum and hence would not reveal evidence of lateral infarction. In Lead V_1 there was a QR complex, elevated RS-T junction, and inverted T wave much like the findings in aV_L. The pattern in Lead V_1 resembled that in the corresponding lead in Case 143 and was attributed to extension of the lateral infarct into the basal portion of the anteroseptal wall of the left ventricle. In the differential diagnosis the possibility of right ventricular hypertrophy was considered because of the prominent initial R wave in aV_R, the late upright deflection in V_1, and the prominent S wave in the remaining precordial leads.[15] Although right ventricular hypertrophy may be responsible for a small Q wave in precordial leads over the right ventricle, it should at the same time produce a much larger R wave than that present in Lead V_1 of this patient, along with depression, rather than elevation, of the RS-T junction. The pattern in Lead V_1 was thus considered to be much more consistent with infarction than with right ventricular hypertrophy. From the RST-T pattern in Leads aV_L and V_1, the infarct was considered of recent origin.

Pathologic Findings.—The heart weighed 562 grams and exhibited left ventricular hypertrophy. A recent infarct was found in the basal one-half of the lateral wall and was comparable in size and position to the lesion of the two basilar segments in Case 143 (Fig. 7), except that it

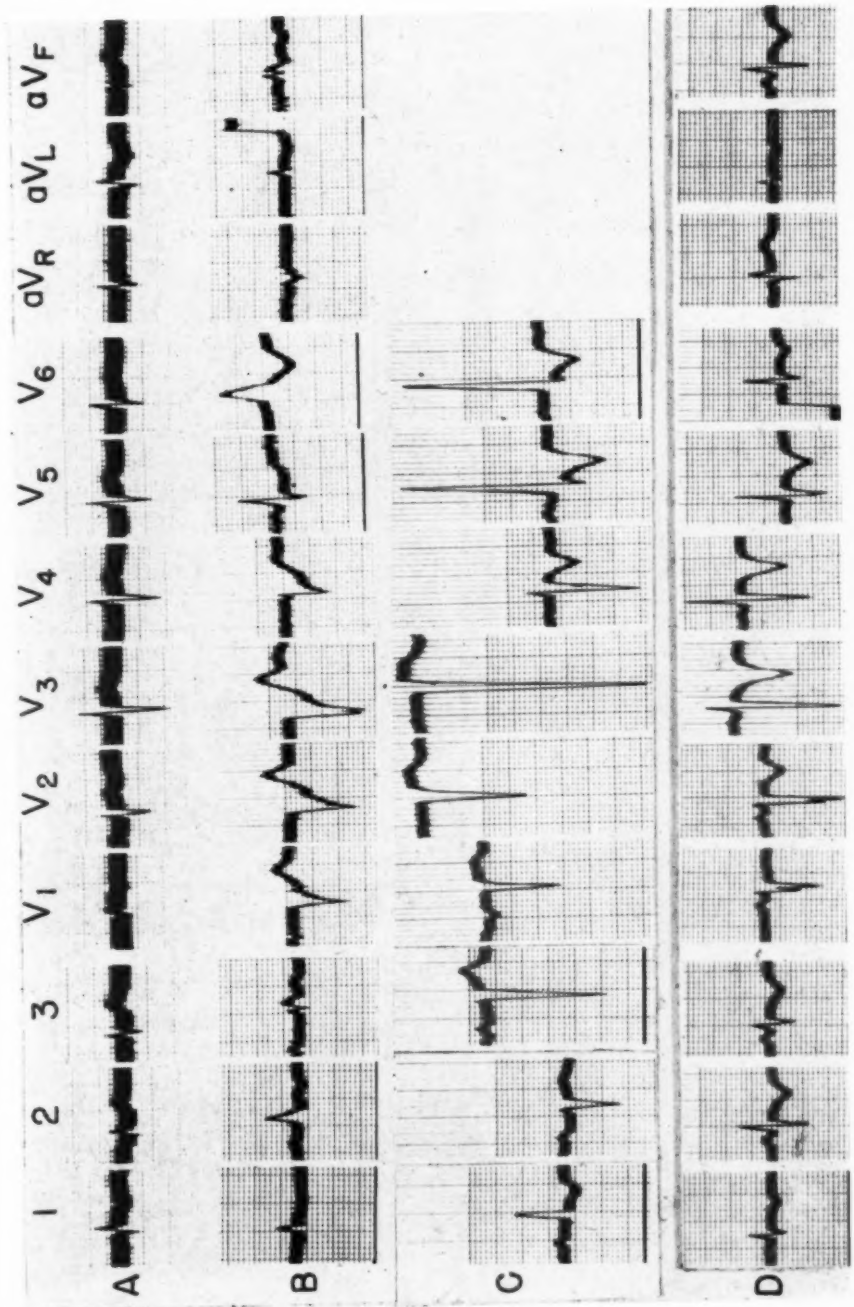

Fig. 12.—Electrocardiograms in lateral infarction. *A*, Case 147; *B*, Case 148; *C*, Case 149; *D*, Case 150.

extended slightly farther into the anterior wall. The infarct tapered toward a blunted point in the mid-portion of the lateral wall. No evidence was found of infarction of the septum or right ventricle. There was good correlation between the infarct of the basal portion of the lateral wall and the QR pattern in Lead aV_L. Since no other explanation was found for the abnormal QR pattern in V_1, it may be have been a manifestation of the continuation of the infarct into the basilar portion of the anterolateral wall.

CASE 148.—A 73-year-old man gave a history of intermittent attacks of retrosternal pain and dyspnea, which were brief in duration, until the evening prior to hospital admission. At that time he was seized with a much more severe attack which lasted all night. He was admitted in shock and remained in severe circulatory collapse until his death four days later.

Electrocardiographic Findings.—An electrocardiogram, obtained two hours after admission and following the administration of 1.6 mg. of Cedilanid, is reproduced in Fig. 12,*B*. There was an underlying sinus rhythm with P-R interval of 0.30 to 0.32 second, complicated by episodes of escaped ventricular rhythm with interference dissociation. The abnormalities in rhythm may have been a result of the Cedilanid. The striking feature of the precordial leads was the very marked RS-T depression in Leads V_2 through V_4 and moderate depression in V_1 and V_5. It was believed that this was independent of Cedilanid action because the Q-T interval was well above the limits of normal and because digitalis glycosides tend to produce elevation of the RS-T segment in leads where the major portion of the QRS complex is downward and depression in leads where the major portion of the QRS is upright. Two possibilities remained for consideration: (1) acute infarction or ischemia of the subendocardial portion of the anteroseptal wall of the left ventricle, and (2) a reciprocal pattern secondary to recent posterolateral infarction. Because of the presence of a definite initial R wave in Lead V_{3R} and a slurred or notched QS complex in V_1 through V_4, an ante-mortem diagnosis was made of a recent infarct involving chiefly the subendocardial portion of the anteroseptal wall of the left ventricle. In addition, the presence of a posterolateral infarct was suspected from the findings in Leads V_6, aV_L, and aV_F. In cycles of supraventricular origin in Lead aV_F, there was a coarsely notched M-shaped QRS complex measuring 0.15 second in duration, a longer duration than was present in any other unipolar lead. This was interpreted as evidence of a conduction defect in the posterior wall of the left ventricle of a type which could be due to fibrosis from remote infarction. The RS-T segment in Leads aV_F, aV_L, and V_6 was isoelectric to slightly elevated and showed a distinct upward bowing, and ended in a shallowly inverted T wave. The contour of the RS-T segment and T wave in these leads was atypical of Cedilanid and suggestive of a lesion of the subepicardial portion of the lateral wall, but the findings were considered too meager to justify a definite diagnosis. The electrocardiogram was therefore interpreted as indicating a recent infarct of the subendocardial portion of the anteroseptal wall of the left ventricle which extended into the left side of the septum and was probably accompanied by an old lesion in the posterior wall, perhaps the result of infarction. Unfortunately, no further tracings were obtained.

Pathologic Findings.—The heart weighed 442 grams and revealed a large recent infarct occupying the entire lateral wall. The involvement of the basilar one-half of the lateral wall was comparable to that of the recent infarct in Case 153 (Fig. 17). The recent lesion continued into the basilar one-half of the posterolateral wall, where it was confluent with an old, patchy fibrosis, resulting from an old, healed posterobasal infarct. It its apical portion, the recent infarct extended diagonally forward to involve the subendocardial one-half of the anterolateral wall. The unusual RST-T pattern in Leads V_6 and aV_L was probably a manifestation of the recent lateral infarct. The lack of a diagnostic QRS pattern in V_6 and aV_L might have been due to patchy distribution of the lesion at the time the electrocardiogram was taken, with subsequent confluence as a result of a persistent shocklike state during the next four days. If the RS-T depression in the first four precordial leads had been merely a reciprocal manifestation of the recent posterolateral infarct, a definite, if not exaggerated, initial R wave would have been expected in these leads. No evidence of anteroseptal infarct was found at autopsy to account for the abnormal QS complexes in these leads. Since the infarct extended into the subendocardial portion of the lateral one-half of the anterior wall, a moderate counterclockwise rotation might have permitted transmission of the potentials of the infarcted region to the anterior chest wall, thereby

making the pattern in V_2 through V_4 a direct manifestation of the infarct. The depression of the RS-T segment in these leads may have been augmented as a result of the reciprocal effects of the recent posterolateral infarct. The fibrosis of the posterior wall could have explained the broad M-shaped QRS complex in Lead aV_F and may have been responsible for the broadening of the S wave in the first four precordial leads.

CASE 149.—A 64-year-old man had had no cardiovascular symptoms until two weeks before hospital admission, when he was suddenly stricken with severe dyspnea while climbing one flight of stairs. Thoracic pain was denied. Progressive cardiac failure occurred during the next fortnight, leading to admission. While in the hospital, he had several attacks of auricular tachycardia with prolonged P-R interval. The last attack caused recurrence of heart failure and death on the thirty-seventh hospital day.

Electrocardiographic Findings.—An electrocardiogram obtained on the twenty-second day, while the patient was taking maintenance doses of digitalis, is reproduced in Fig. 12,*C*. The QRS pattern in the precordial and limb leads was essentially the same as that in five other tracings taken at intervals during his five-week hospital stay. The tall R wave and slightly delayed intrinsicoid deflection in Leads V_5 and V_6 were indicative of left ventricular hypertrophy. Serial tracings revealed gradually increasing RS-T depression in Leads V_5 and V_6 together with progressive deepening of the consistently inverted T waves. It was believed that left ventricular hypertrophy was basically responsible for the depression of the RS-T segment and negativity of the T wave, and the question arose as to whether the progression was due entirely to digitalis or in part to a lesion of the subendocardial portion of the lateral wall. Because of the patient's condition, digitalis could not be withheld for a period long enough to settle this question. Lead aV_L closely resembled V_6, whereas aV_F showed small R and deep S waves due to horizontal position. The QS complex consistently recorded in V_1, V_2, and V_3 may have been due to anteroseptal infarction or may have constituted a variant occasionally found in uncomplicated left ventricular hypertrophy. Although recent anteroseptal infarct seemed excluded by the absence of significant serial changes in the T wave, a positive differentiation between old, healed anteroseptal infarction and uncomplicated left ventricular hypertrophy was not made. Thus, the only definite diagnosis made from the electrocardiogram was left ventricular hypertrophy with digitalis effect, but the possibilities of old, healed anteroseptal infarct and a more recent lesion confined to the subendocardial portion of the lateral wall were seriously considered.

Pathologic Findings.—The heart weighed 694 grams as a result of left ventricular hypertrophy secondary to rheumatic aortic stenosis. A relatively small organizing infarct was found, confined to the subendocardial one-fourth of the lateral wall in the middle one-third of the left ventricle. The position and size of this infarct corresponded closely with that in the third and fourth segments in Case 144 (Fig. 8). It is possible that this infarct was in part responsible for the progressive depression of the RS-T junction and deepening of the inverted T wave in Leads V_5 and V_6. The absence of Q waves from these leads was probably due to the relatively small size of the infarct in comparison with the bulk of the surrounding hypertrophied, but uninfarcted, anterolateral wall. Since there was no evidence of anteroseptal infarction, the QS complex in Leads V_1, V_2, and V_3 was apparently a variant sometimes encountered in left ventricular hypertrophy.

CASE 150.—A 65-year-old man gave a history of shortness of breath on exertion for five years, but continued to work as machinist until a few days before hospital admission, when he was completely incapacitated because of an abrupt increase in dyspnea. Thoracic pain was denied. He was admitted in congestive heart failure and died four days later.

Electrocardiographic Findings.—An electrocardiogram obtained on the second hospital day, after the administration of 1.6 mg. of Cedilanid, is reproduced in Fig. 12,*D*. In all precordial leads, in aV_L, and in aV_F the initial deflection was upright and the QRS complex was considered to be within the limits of normal. The striking feature was the deeply inverted T wave with isoelectric RS-T junction in Leads V_2 through V_6, in Lead aV_F, and in the standard leads. Because of the contour of the RS-T segment and T wave and the relatively long Q-T interval, the abnormalities in the RS-T complex were not due primarily to Cedilanid. The widespread distribution of the inverted T wave, as well as its contour and depth, was typical of a diffuse lesion of the sub-

epicardial layer, maximal in the anterolateral wall of the left ventricle. The ante-mortem electrocardiographic diagnosis rested between pericarditis and a subepicardial infarct.

Pathologic Findings.—The heart weighed 400 grams and showed definite evidence of right ventricular dilatation and hypertrophy secondary to obstructive emphysema. There was no gross evidence of pericarditis. Multiple microscopic blocks showed an extensive subepicardial lesion which involved the entire lateral wall and overlapped onto the anterior and posterior walls of the left ventricle, corresponding closely in position and surface area to the entire infarct of the outer wall of the left ventricle in Case 153 (Fig. 17). In all microscopic blocks the lesion was limited to the subepicardial layer and was considered to be the result of infarction rather than inflammation. The deep inversion of the T waves and the normal QRS pattern in Leads V_2 through V_6 and aV_F corresponded satisfactorily with the subepicardial infarct found at autopsy. The right ventricular hypertrophy was missed electrocardiographically because of the absence of diagnostic changes in the QRS complex.* The low upright T wave in right ventricular Lead V_1 indicated that the T-wave inversion of the other leads was independent of right ventricular hypertrophy.

CASE 151.—A 70-year-old man was admitted to Grace Hospital in cardiac failure on March 19, 1946, with a history of shortness of breath for one week and tightness in the chest and pain in the left shoulder and arm for one day. He was readmitted on May 27, 1946, because of vise-like precordial pain of two days' duration and had a clinical course compatible with myocardial infarction. Digitalis was instituted and maintained for the rest of his life. Ever since discharge, he was partially incapacitated because of exertional and paroxysmal nocturnal dyspnea. He was admitted to Receiving Hospital in shock on Feb. 26, 1947, eighteen hours after the onset of a third attack of prolonged retrosternal pain. Death occurred one week later.

Electrocardiographic Findings.—An electrocardiogram† obtained on March 19, 1946, before the administration of digitalis, and two subsequent tracings, while the patient was on maintenance doses, are reproduced in Fig. 13. In the first five precordial leads on March 19, 1946, an initial upright deflection was registered, whereas in V_6 there was a 2.5 mm. Q wave which was 0.03 second in duration and 33 per cent of the amplitude of the succeeding R wave. This Q wave and the slurred ascending limb of the R wave, which was 0.04 second in duration, were considered abnormal and referable to infarction of the subendocardial portion of the lateral wall. The standard leads showed marked left axis deviation with pronounced slurring or notching, but were not diagnostic of infarction. In Lead V_6 obtained on June 4, 1946, the Q wave was smaller, but the QR complex was still abnormal, though no longer diagnostic of lateral infarction. The T wave in this lead displayed signs of digitalis effect. The most striking change took place in Leads V_2 through V_4 and consisted in sharp inversion of the T wave, without significant difference in the QRS complex. The reversal in direction of the T wave in these leads was not due solely to digitalis, since the effect of this drug on a pattern like that recorded in Leads V_2 through V_4 on March 19 is to cause further elevation of the RS-T junction, straightening of the RS-T segment, and increase in the amplitude of the upright T wave, along with reduction in the QT interval. The underlying cause for the reversal in these T waves may have been an intramural anteroseptal infarction, an anteroseptal ischemic zone consequent upon extension of the lateral infarct high in the basal portion of anterolateral wall, or acute right ventricular dilatation. The latter was unlikely because of the fact that the T-wave inversion was not nearly as deep in V_1 as in leads farther to the left. Leads V_1 to V_3 recorded on March 3, 1947, showed RS complexes comparable to those in the same leads of previous tracings. The formerly inverted T waves in these leads had become upright. On the other hand, the slurred QS complex recorded in Lead V_4 and the abnormal QR complex in V_5 differed significantly from the findings in previous records and indicated that infarction of the anterior and anterolateral wall of the left apex had occurred some time since the tracing of June 4, 1946. The T-wave pattern in these leads was not characteristic of recent

*This case was previously reported as Case 38 of a paper on right ventricular hypertrophy.[15]

†The first two electrocardiograms and the information relevant to his course at Grace Hospital were furnished through the courtesy of Dr. L. T. Colvin. The record of Lead V_2 on March 19, 1946, was the only cycle available on the chart and showed a much broader QRS complex than in other leads, suggesting that it was a ventricular premature beat.

infarction and might have been the result of digitalis. No significant change had occurred in the QRS complex of Lead V_6. To investigate further the possibility of a high lateral infarct, tracings were obtained above precordial Positions 4, 5, and 6 on a horizontal line at the level of the junction of the third intercostal space and sternum. The records taken above Positions 4 and 5 resembled closely the QR complex registered at the customary fifth precordial position. The tracing high in the mid-axillary line above Position 6 was characterized by a Q wave of 2.0 mm., an R wave of 5.0 mm., an isoelectric RS-T junction, convex upward RS-T segment, and inverted T wave. The QR pattern in this lead was thus more abnormal than in either the customary Lead V_6 or Lead aV_L, and suggested that the infarct extended high in the subendocardial portion of the lateral wall.

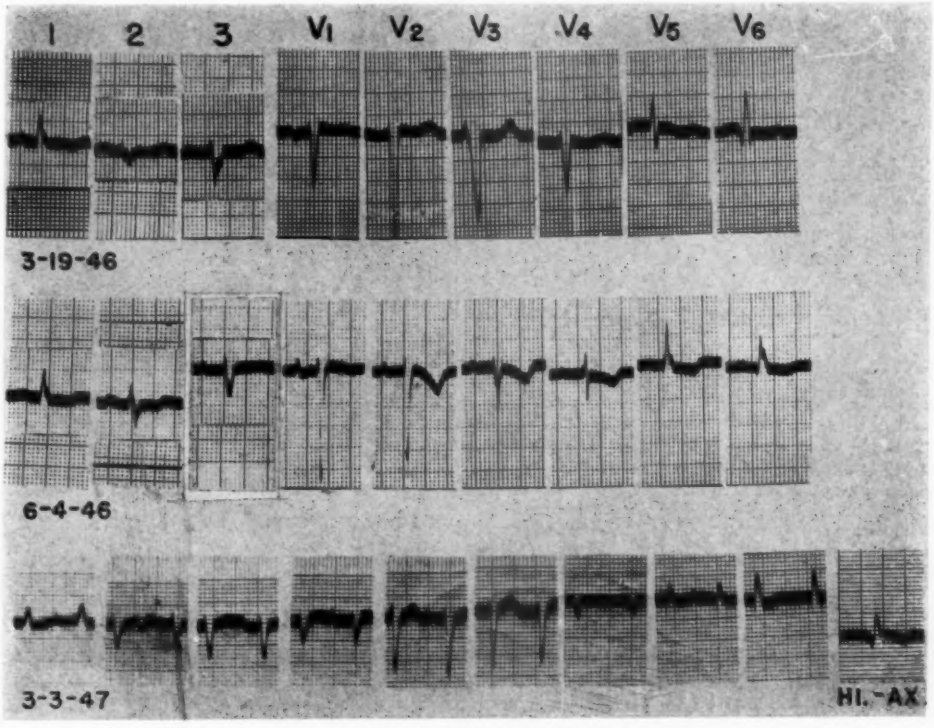

Fig. 13.—Serial electrocardiograms in Case 151.

Pathologic Findings.—The heart weighed 562 grams and exhibited an old, healed infarct of the entire lateral wall and a recent infarct of the subendocardial portion of the anterior wall and left side of the septum. The old infarct occupied the posterolateral aspect of the apex and extended diagonally forward and upward so as to involve the anterolateral wall at the base where the wall was thin and outpouched to form a ventricular aneurysm, as represented by the broken lines of Fig. 14. The position of the recent infarct was outlined by solid lines. Microscopic sections showed that the old infarct involved almost the entire thickness of the wall, whereas the recent infarct was limited to the subendocardial one-half. The old infarct of the lateral wall was probably responsible for the abnormal QR pattern in Lead V_6 recorded on March 19, 1946. An extension into the anterolateral portion of the fifth and sixth segments on May 25, 1946, seemed the best explanation for the reversal of the T waves in Leads V_2, V_3, and V_4 recorded on June 4, 1946. According to this hypothesis, the findings in these leads were representative of an outlying ischemic zone. The findings in Lead V_6 and the high axillary lead of the final tracing

were probably a residue of the old infarct, whereas those in V_4 and V_5 were presumably the result of the more recent anteroapical infarct. Leads V_1, V_2, and V_3 gave no definite indication of the involvement of the left side of the septum. The extension of the old infarct into the posterolateral wall of the apex was not revealed by the standard leads on any occasion or by Lead aV_F on the final admission.

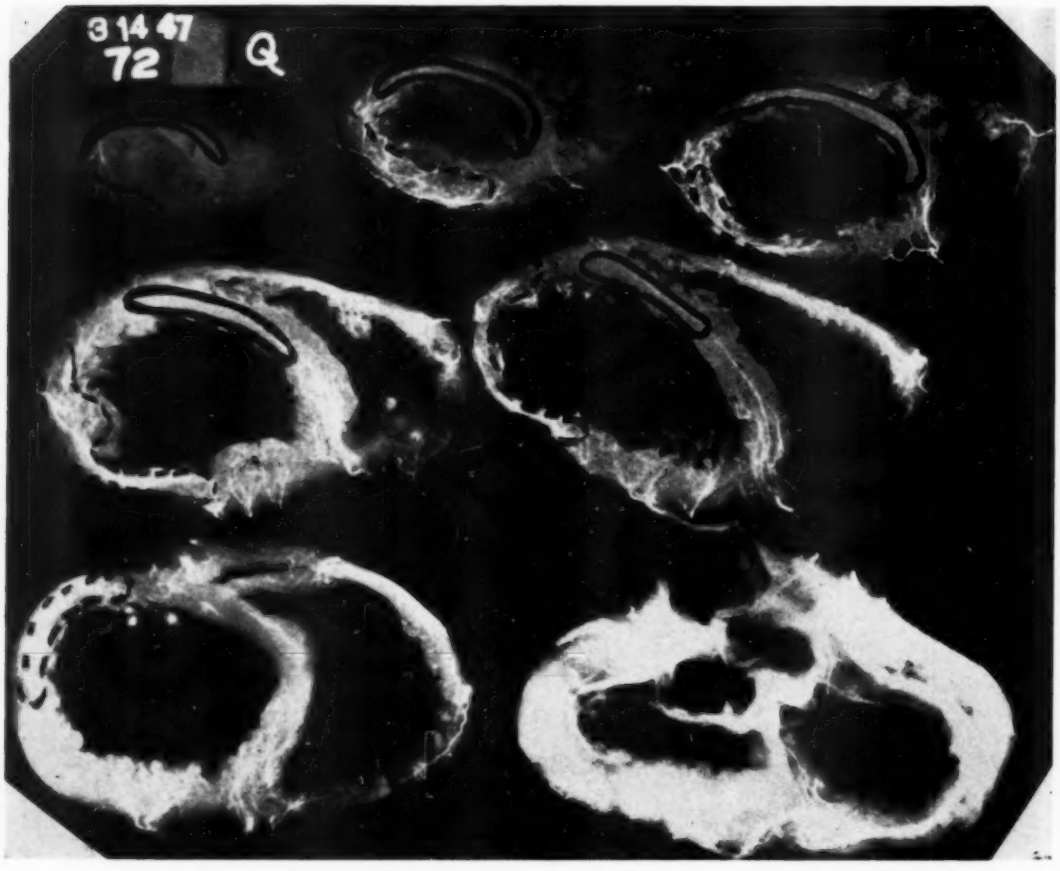

Fig. 14.—Roentgenogram of the injected heart in Case 151, showing recent anteroseptal infarct in solid outline and old, healed lateral infarct in broken lines.

CASE 152.—A 59-year-old man gave a typical history of angina pectoris, beginning in October, 1942, and myocardial infarction, occurring in November, 1943. His second attack of prolonged retrosternal pain began on March 10, 1944, and led to hospitalization in congestive failure the next day. He was given 1.6 mg. of Cedilanid soon after admission, but received no further cardiac glycosides until March 26, when digitalization was carried out and maintained for the rest of his life. His third attack of prolonged retrosternal pain began on May 17, 1944, and led to readmission in shock the following day. Death occurred twenty-five hours after admission.

Electrocardiographic Findings.—Electrocardiograms reproduced in Fig. 15 were obtained on March 13, three days after the onset of the second attack of prolonged retrosternal pain, on April 22, while the patient was under observation in the out-patient department, and on May 19, two days after the onset of his third attack. The QRS complex was 0.12 second in duration and was slurred or notched abnormally in several leads. The conduction defect was located in

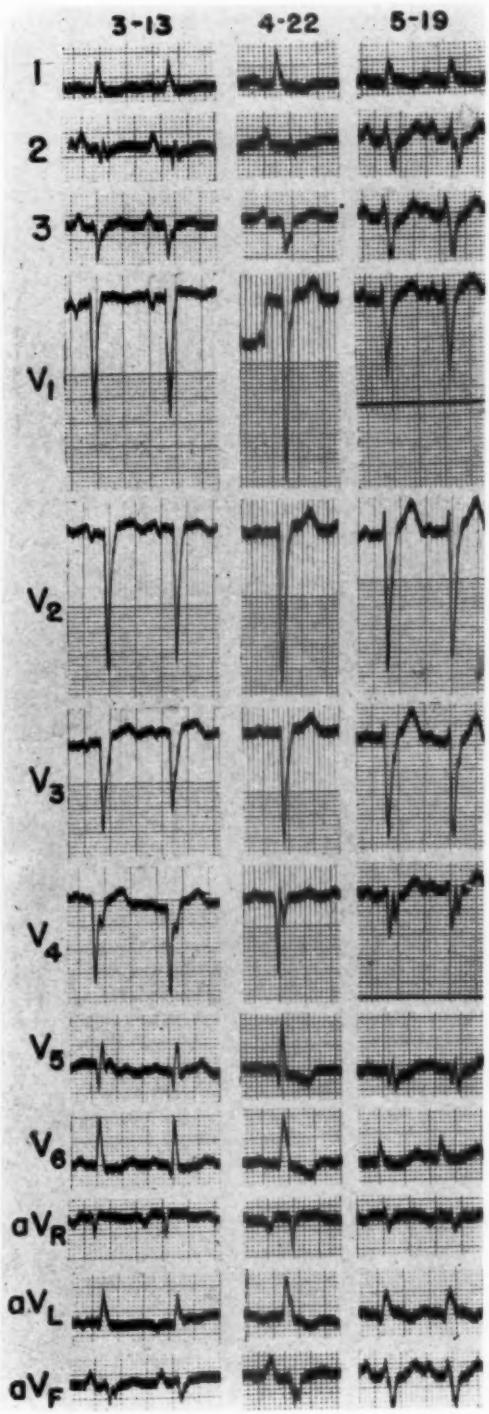

Fig. 15.—Serial electrocardiograms in Case 152.

the left ventricle, because of the delayed onset of the intrinsicoid deflection in Lead V_6, and was attributed to anterolateral infarction, because of the abnormal QR pattern in V_5. In the first four precordial leads, the electrode was judged to be to the right of the interventricular septum, because of the minute R wave and the deep, broad, slurred S wave. The most significant features of the pattern in the first three precordial leads were an initial Q wave 0.5 to 1.0 mm. in depth and the diminishing height of the R wave as the electrode was moved toward the left. These findings were interpreted as evidence of continuation of the anterolateral infarct into the left side of the interventricular septum. From the RST-T contour in the tracing of March 13, it was thought that the infarct was old and healed. However, two tracings taken during the next ten days revealed no significant change in the QRS contour, but showed progressive inversion of the T waves in Leads V_5, V_6, aV_L, and Lead I, to reach a pattern comparable to that in the tracing of April 22. Since no cardiac glycosides were given during this period, drug effects were excluded. The T-wave evolution pointed to a recent anterolateral infarction, which may have been superimposed on an older lesion in the same area. The minute, slurred R wave and broad, notched S wave consistently recorded in Lead aV_F were presumably transmitted from the posteroinferior surface of the right ventricle as a result of horizontal position of the heart. To investigate the possibility of posterior infarction, esophageal leads were obtained on April 22. Records from the ventricular level showed a small Q wave which ranged from 8 to 33 per cent of the succeeding R wave. Although the Q/R ratio was not definitely abnormal, the fact that the Q wave was accompanied by coarse notching of the R wave was strongly suggestive of a patchy lesion in the posterior wall. In the final tracing, the most striking change occurred in Lead aV_L and secondarily in Lead I. It was characterized by the appearance of a slurred Q wave 0.03 second in duration, by a significant reduction in the amplitude of the R wave, and by upward displacement of a formerly depressed RS-T junction. These changes, along with the marked reduction in the amplitude of the R wave in Leads V_5 and V_6 and the reciprocal increase in the R and T waves of aV_F and the first three precordial leads, were diagnostic of acute reinfarction of the lateral wall of the left ventricle.

Pathologic Findings.—The heart weighed 614 grams and revealed a recent lateral infarct almost identical in size, shape, and position with the recent infarct in Case 142 (Fig. 6). In addition, an old, healed subendocardial anteroposterior infarct was found, involving the subendocardial one-half of the entire posterior wall, the apical one-third of the anterior and lateral walls, and the apical one-half of the left side of the septum. The abnormal pattern in Leads V_5 and V_6 of the early tracings could be correlated with the anterolateral portion of the old infarct, whereas the initial Q wave in V_1, V_2, and V_3 was apparently a manifestation of involvement of the left side of the septum. The absence of diagnostic signs of the posterior infarction in Lead aV_F was probably the result of horizontal position of the heart with reference of the potential variations of the posterior inferior surface of the right ventricle to the left leg. The Q and notched R waves recorded in esophageal leads at the ventricular level were probably a manifestation of the posterior infarction, but the Q/R ratio was lower than would have been expected from a lesion involving the subendocardial one-half of the wall. The recent lateral infarct was found chiefly in the subendocardial one-half, but extended in fingerlike fashion to the epicardium. The changes in Leads I, aV_L, V_5, and V_6 of the final tracing could be correlated with the terminal lateral infarct.

CASE 153.—A 65-year-old woman gave a history of myocardial infarction in 1935, from which she made an uneventful recovery, remaining symptom free until 1940. After three years of gradually increasing dyspnea, congestive failure occurred, necessitating hospitalization in October, 1943. Digitalization was carried out and continued for the rest of her life. Compensation was maintained until Jan. 6, 1944, when there was a sudden recurrence of dyspnea without associated chest pain, followed by progressive cardiac failure during the next two weeks. She was readmitted in extreme decompensation on Jan. 19, 1944, and died two weeks later.

Electrocardiographic Findings.—Electrocardiograms from the two hospital admissions are reproduced in Fig. 16. On Oct. 21, 1943, the QRS complex measured 0.12 second and was notched or slurred in a number of leads, thus establishing the presence of an intraventricular conduction defect. The time interval of 0.07 to 0.08 second from onset of the QRS complex to the beginning

of the intrinsicoid deflection in Leads V_5 and V_6 signified a delay in conduction of the impulse through the left ventricle. The Q waves preceding the later intrinsicoid deflections in these leads excluded uncomplicated left bundle branch block and were typical of a conduction defect in the anterolateral wall of the left ventricle. Left bundle branch block associated with complete destruction of the septum was considered in the differential diagnosis, but was ruled out by insufficient prolongation of the QRS complex. Although the Q/R ratio in Lead V_5 was only 15 per cent, the Q wave was abnormal because of the 0.03 second interval from onset to nadir, and

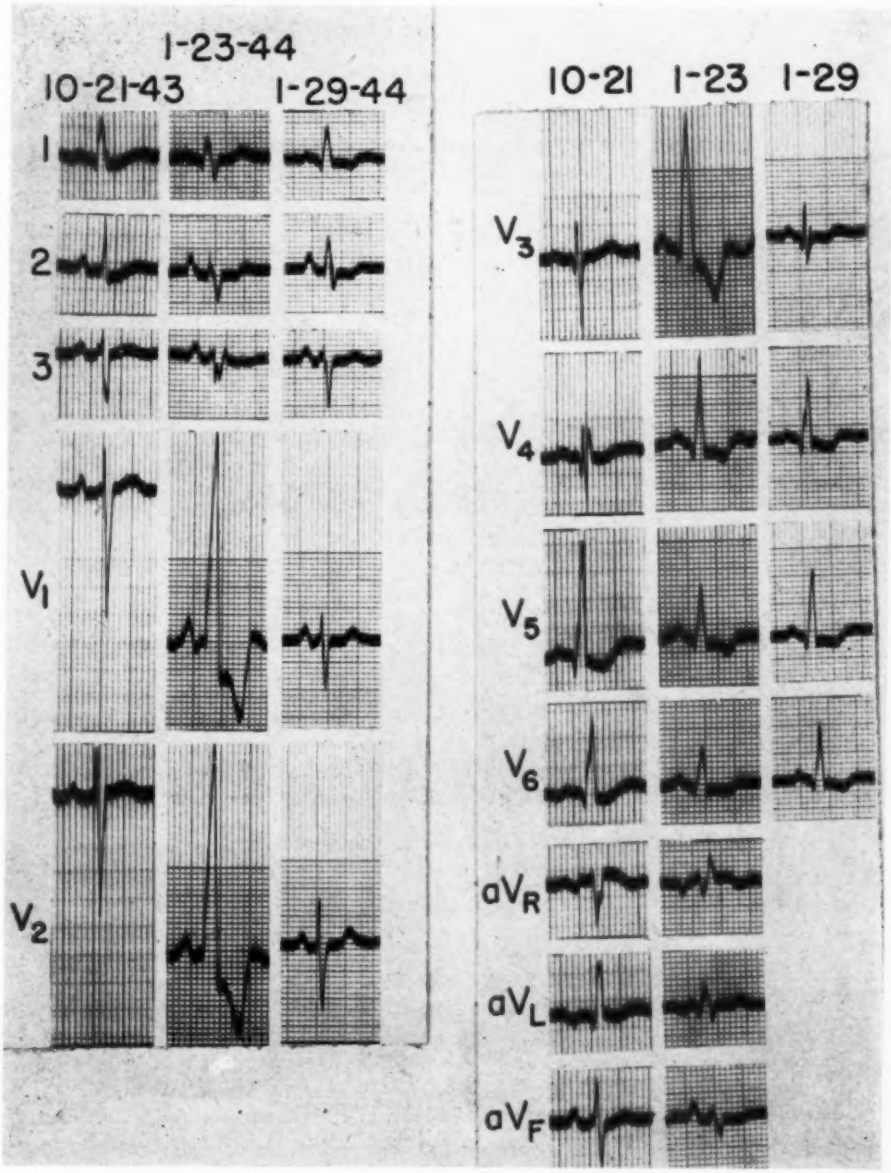

Fig. 16.—Serial electrocardiograms in Case 153.

the R wave was abnormal because of the coarse slurring and the 0.05 second interval between its onset and peak. A QR complex in Leads V_5 and V_6 characterized by a prolonged Q wave and an abnormally broad, slurred, or notched upstroke was regarded as a typical manifestation of anterolateral infarction, densely distributed in the subendocardial layer and patchy in the remainder of the wall. The association of a Q wave and notched R wave pointed more toward old than recent infarction. However, positive conclusions as to the age of the lesion on the first admission were not justifiable from the electrocardiographic findings alone, since the RS-T complex was distorted by digitalis action in the single record obtained. The presence of a Q wave and abnormal Q/R ratio in V_3 and V_4 and the fact that the upright deflection in these leads was smaller than the initial R wave of right ventricular Leads V_1 and V_2 constituted evidence that the infarct extended subendocardially into the apical portion of the anteroseptal aspect of the left ventricle. The inverted P wave in Lead aV_L suggested that the QR complex may have been transmitted from the posterobasal rather than the lateral wall of the left ventricle and thus left the

Fig. 17.—Roentgenogram of the injected heart in Case 153, showing position of recent high lateral infarct and old anterolateral posterior apical infarct.

interpretation of the findings in aV_L and Lead I in doubt. In the tracing of Jan. 23, 1944, the QRS interval had increased to 0.16 second and a striking change had occurred in the QRS-T pattern of Leads V_1 through V_3, characterized by the appearance of a very tall R wave, markedly depressed RS-T junction, and deeply inverted T wave. On the other hand, the QRS pattern in Leads V_5 and V_6 showed no significant change apart from a 50 per cent reduction in the voltage of the R wave. The upright initial deflection in V_1 and V_2, together with the delay of the intrinsicoid deflection in these leads to 0.08 second, indicated that the newly developed conduction defect was in the right side of the septum and consisted of right bundle branch block. Since the P-R interval on January 23 was 0.16 second, the possibility of an intermittent Wolff-Parkinson-White syndrome was excluded. The development of the right bundle branch block was manifested by the appearance of a late S wave in aV_L, a late R wave in aV_R, and a late S wave in Lead I. The absence of a late S wave in Leads V_5 and V_6 was unusual, but was probably due to the coexistent

conduction defect in the outer wall of the left ventricle. The transient reduction in the amplitude of the R wave in Leads V_5, V_6, and aV_L could have been secondary to the right bundle branch block and thus could not be accepted as evidence of a left ventricular lesion. The sudden development of right bundle branch block was suggestive of infarction of the septum, but the subsequent disappearance, together with the return to a pattern, on Jan. 29, 1944, much like that in the original tracing, raised doubt as to the cause of the right bundle branch block. It is noteworthy that the pattern on Jan. 29, 1944, was almost identical with that of October 21 except in V_3 and V_4, where the differences were attributable to a shift in transitional zone. Digitalis effects upon the RS-T segment and T wave were less marked in the last than in the first tracing.

Pathologic Findings.—The heart weighed 470 grams and exhibited on old, completely healed infarct involving the apical one-half of the anteroseptal wall of the left ventricle and the apical one-third of the lateral and posterior walls and the left side of the septum, together with a recent infarct of the basal two-thirds of the lateral wall and the interventricular septum, as outlined in Fig. 17. The old infarct had caused dense fibrosis of the subendocardial one-half of the free wall of the left apex and very patchy fibrosis of the subepicardial one-half. Thus, the findings in Leads V_5 and V_6 corresponded closely with the old infarct of the apical portion of the lateral wall, whereas those in V_3 and V_4 conformed with the anteroseptal lesion. No signs of extension into the posterior aspect of the apex were evident in Leads II, III, or aV_F, apparently because the heart was in a horizontal position. The old infarct of the apical portion of the interventricular septum was not detected electrocardiographically. The recent infarct of the basal two-thirds of the septum could have produced right bundle branch block, but the transient duration of the conduction defect made it necessary to consider a functional lesion associated with cardiac failure as an alternative possibility. The recent infarct of the basal two-thirds of the lateral wall was confined to the subendocardial one-half of the wall and was not diagnosed from the electrocardiograms of Jan. 23 and Jan. 29, 1944. It is noteworthy that this lesion caused no significant change in the QRS pattern in Leads V_5 or V_6. The high lateral infarct might have been detected if high precordial and axillary leads at the level of the third intercostal space had been taken. This case well demonstrates the inadequacy of the customary precordial leads in the diagnosis of high lateral infarction.

CASE 154.—A 48-year-old woman was first admitted in December, 1946, because of pneumonia. She gave a history of sudden onset of severe precordial pain and dyspnea in 1944 and a second attack in August, 1945, both treated by prolonged bed rest at home. Digitalis had been maintained ever since and was increased in April, 1947, because of congestive failure. Toxic psychosis developed, leading to readmission. Death occurred on the tenth hospital day.

Electrocardiographic Findings.—An electrocardiogram obtained three days before death is reproduced in Fig. 18,*A*. The QRS-T pattern in this tracing was similar to that in three previous tracings taken during the first admission. The QRS interval measured 0.12 second. The distinct Q wave and late intrinsicoid deflection in Lead V_6 aroused the suspicion of infarction of the subendocardial portion of the lateral wall, but could have been a manifestation of uncomplicated left ventricular hypertrophy. The findings in Lead aV_L were more distinctive. The Q/R ratio of 30 per cent, the notched upstroke, and the 0.075 second interval preceding the intrinsicoid deflection were representative of the type of conduction defect of the outer wall produced by patchy infarction. Although the suggestion of an initial negative phase preceding the upright P wave in aV_L would ordinarily raise the question of transmission of the potential variations of the posterobasal aspect of the heart to the left arm, the close resemblance of the P wave in aV_L to that in Lead V_6 indicated a common pathway through the lateral wall of the left ventricle. Therefore, it was concluded that the Q wave and notched upstroke in Lead aV_L were due to lateral infarction involving the subendocardial layer and distributed in a patchy manner through the remainder of the wall. This pattern carried over into Lead I, which was strongly suggestive of lateral infarction. The initial phase of the QRS complex was upright in the first five precordial leads. The decrease in the amplitude of the R wave from 10.0 mm. in V_2 and V_3 to 5.0 mm. in V_4 and V_5 raised the question of anteroseptal infarction, but might have been merely a transitional phenomenon. The depression of the RS-T junction and straightening of the segment following the tall

R wave of Leads V_6 and aV_L and the reciprocal upward displacement and straightening of the RS-T segment following the deep S wave of the first four precordial leads were attributed to the superimposed effects of full digitalization.

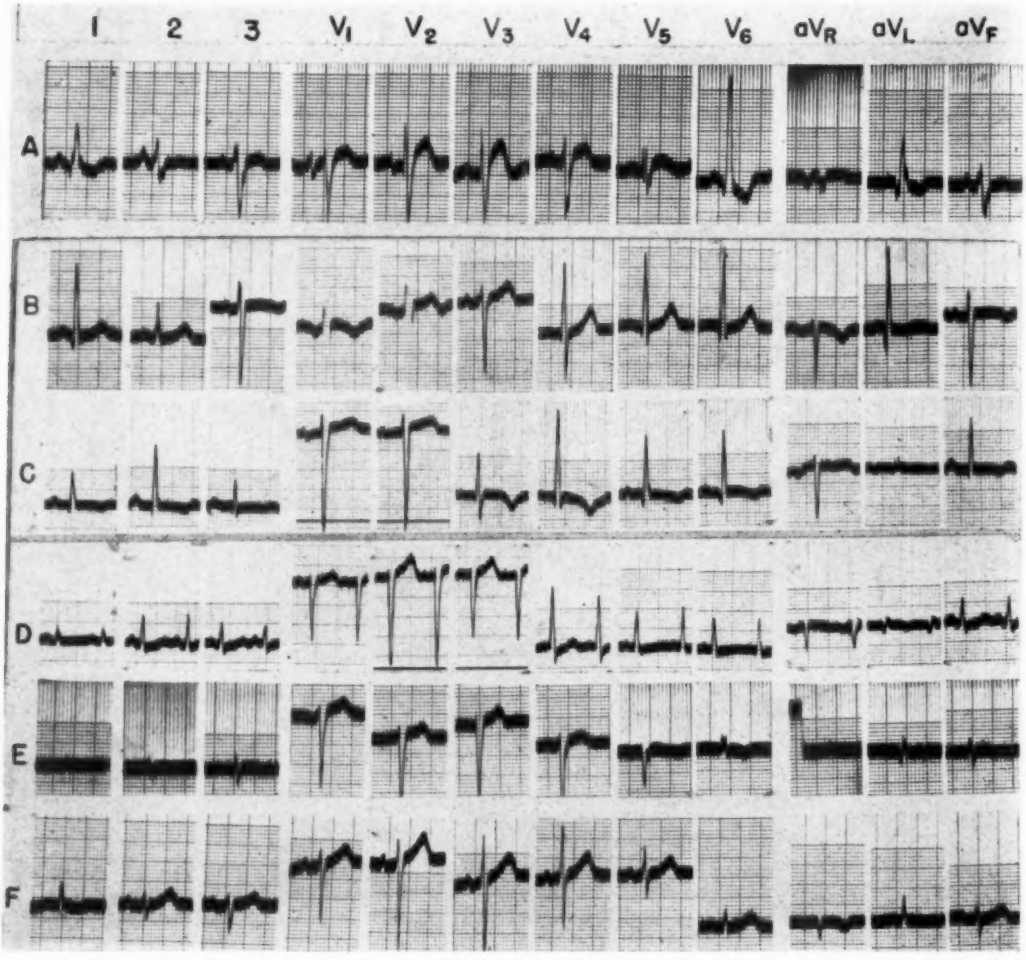

Fig. 18.—Electrocardiograms in old, healed lateral infarct. *A*, Case 154; *B*, Case 156; *C*, Case 157; *D*, Case 158; *E*, Case 160; *F*, Case 161.

Pathologic Findings.—The heart weighed 475 grams and revealed an old, completely healed lateral infarct, closely comparable in size and position to the lesion in Case 145 (Fig. 9). The resultant fibrosis was dense in the subendocardial one-fourth to one-half and very patchy in the remainder of the wall. There was good correspondence between the findings in Lead aV_L and the old, high lateral infarct at autopsy. The borderline pattern in V_6 was compatible with the thin layer of subendocardial infarction in the apical portion of the lateral wall. The continuation of the infarct into the posterior wall near the apex, in a fashion comparable to that in the second segment of Fig. 9, was not detected in Lead aV_F because of the horizontal position of the heart.

CASE 155.—A 72-year-old man gave a typical history of myocardial infarction nine months prior to hospital admission. Since then he had had repeated paroxysms of nocturnal dyspnea

and had taken digitalis for three months. He was admitted in severe congestive failure and died of bronchopneumonia on the sixth day.

Electrocardiographic Findings.—An electrocardiogram was obtained thirteen hours after admission, but is not reproduced because of its close resemblance to that in Case 154 (Fig. 18,*A*). The QRS complex in Leads V_1, V_2, and V_3 was comparable to that in the corresponding leads in Case 154 and a multiphasic transitional complex was recorded in Lead V_4, resembling that in V_5 (Fig. 18,*A*). The combination of the QRS interval of 0.12 second with a QR pattern and late intrinsicoid deflection in Leads V_5, V_6, and aV_L was indicative of a conduction defect in the anterolateral wall of the left ventricle. In Lead V_5 the Q wave was only 0.02 second in duration, but was followed by coarse notching near the base of the ascending limb of the R wave and an abnormally long (0.05 second) interval from onset to peak of the R wave. In Lead aV_L a comparable notch appeared on the descending limb of the Q wave and the interval from onset to nadir of the Q wave was 0.04 second, whereas that from beginning to peak of the R wave was 0.03 second. The findings in V_5 and aV_L were regarded as different manifestations of the same lesion and were attributed to an infarct of the subendocardial portion of the anterolateral wall. The abnormal Q wave of aV_L was absent from Lead I, apparently as the result of greater initial negativity in the right arm. The T-wave pattern was comparable to that in Case 154, but the digitalis effects were not as marked.

Pathologic Findings.—The heart weighed 554 grams and exhibited an old, healed infarct of the subendocardial one-half of the anterolateral aspect of the apex, comparable in size and position to that in Case 138 (Fig. 2). Although the electrocardiograms in Cases 154 and 155 were closely comparable, the subendocardial infarct in the former case involved the entire lateral wall, but chiefly in its basal two-thirds, whereas the subendocardial infarct in this case was limited to the apical one-third. The fact that the infarct extended farther into the anterior wall of the apex in this case may have accounted for the abnormal QR pattern in Lead V_5, as well as in V_5 and aV_L.

CASE 156.—A 65-year-old man was admitted to the [illegible] a history of chronic alcoholism complicated by delirium tremens. He had had [illegible] etrosternal fullness for the last five months, but gave no definite history of myocardial [illegible]e contracted pneumonia and died on the nineteenth hospital day. No cardiac glyco[illegible]en.

Electrocardiographic Findings.—An electrocardiogram obtained on the fourth hospital day is reproduced in Fig. 18,*B*. The initial deflection was upright in the first three precordial leads and measured 4.0 mm. in V_1 and 5.0 mm. in V_2, and decreased to 3.0 mm. in V_3. A minute Q wave of brief duration and a tall R wave were recorded in the last three precordial leads, the Q/R ratio being within normal limits. In Lead aV_L there was a Q wave 0.03 second in duration and 6.0 mm. in depth, or approximately 30 per cent of the succeeding R wave. The interpretation of the findings in aV_L depended upon the decision as to whether the potential variations of the left arm were transmitted chiefly from the lateral or from the posterobasal wall of the left ventricle. The QR complex in Lead aV_L could be considered abnormal if derived from the lateral wall, but at the upper limits of normal if transmitted from the vicinity of the posterior portion of the atrioventricular groove. The lack of a late R wave in Lead aV_R was against the latter, but the suggestion of a minute negative phase prior to the upright P wave made it impossible to definitely exclude transmission from the posterobasal wall. Therefore, the findings in Lead aV_L were regarded as strongly suggestive, but not as diagnostic, of lateral infarction. The findings in the precordial leads, when considered by themselves, were insufficient to justify a diagnosis of infarction, but in view of the interpretation of Lead aV_L, it was possible that the slight reduction in the amplitude of the R wave in V_3 and the minute Q waves in the last three precordial leads may have been the result of a small, patchy anterolateral infarct. There was no evidence in either the RS-T segment or T waves to suggest a recent lesion. The standard leads showed definite left axis deviation, but were not diagnostic of infarction.

Pathologic Findings.—The heart weighed 532 grams as a result of left ventricular hypertrophy. A patchy fibrosis was found in the subendocardial one-half of the anterolateral wall in the apical

three segments, occupying a position comparable to that of the infarct in Case 146 (Fig. 11) in the apical two segments, but more like that in Case 143 (Fig. 7) in the third segment. By microscopic examination, the lesion was believed to be the result of infarction. From the position and patchy character of the lesion, it was probably responsible for the borderline findings in the electrocardiogram.

CASE 157.—A 70-year-old man collapsed on the street and was brought to the hospital with aphasia and right hemiplegia and died of the cerebral vascular accident. Past history was unobtainable. No cardiac glycosides were given.

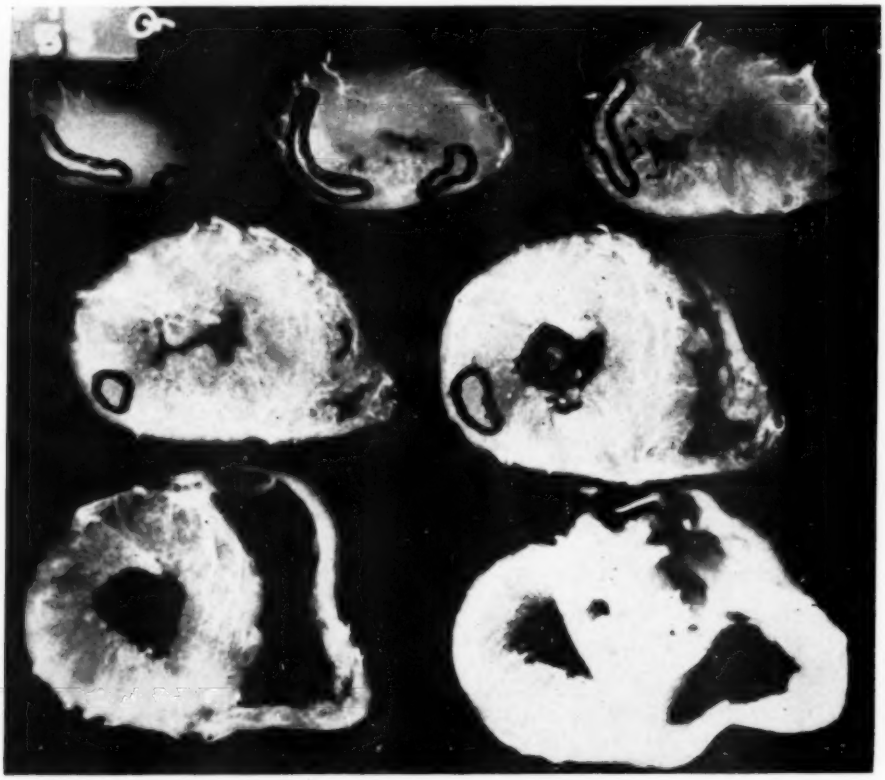

Fig. 19.—Roentgenogram of the injected heart in Case 157.

Electrocardiographic Findings.—An electrocardiogram obtained twenty hours after admission is reproduced in Fig. 18,*C*. The small R and deep S waves in right ventricular Leads V_1 and V_2 and the 2.0 mm. Q wave, tall R wave, and slightly delayed intrinsicoid deflection in left ventricular Leads V_4 through V_6 led to the diagnosis of left ventricular hypertrophy. Although the Q/R ratio in Leads V_4 through V_6 was in keeping with this diagnosis, the interval of 0.03 second from onset to nadir of the Q wave was longer than expected in uncomplicated left ventricular hypertrophy and was strongly suggestive of infarction of a thin layer of subendocardial muscle in the lateral wall of the left ventricle. The RS-T pattern in the last four precordial leads was atypical of left ventricular hypertrophy because of the deeper inversion of the T waves in V_3 and V_4 than in V_5 and V_6 and because of the lack of the expected RS-T depression. The RS-T pattern was compatible with involvement of the subepicardial layer secondary to infarction or localized pericarditis, but further tracings would have been needed to interpret its significance properly. The Q and notched R waves in Lead aV_L would have been strongly suggestive of lateral

infarction if it had been representative of the potential variations of the lateral wall, but the associated negative P waves suggested that cavity potentials may have had a significant effect upon the recordings in Lead aV_L. Thus, the electrocardiographic findings were very suggestive of infarction of the subendocardial portion of the anterolateral wall, but were not sufficiently marked to be pathognomonic.

Pathologic Findings.—The heart weighed 582 grams as a result of left ventricular hypertrophy secondary to aortic stenosis. An old, healed, patchy infarct was found, occupying the subendocardial three-fourths of the lateral and posterolateral walls in the apical three segments and extending into the middle zone of the posterolateral wall in the fourth and fifth segments, as outlined in Fig. 19. This infarct was probably responsible for the QR patterns in Leads V_6 and aV_L, but did not produce definite abnormalities in aV_F. Leads in the posterior axillary line and higher in the axilla might have revealed diagnostic signs. The infarct did not extend far enough forward to explain the deeply inverted T waves in Leads V_3 and V_4. These may have been secondary to the left ventricular hypertrophy or might have resulted from a histologically unrecognized anterior ischemia.

CASE 158.—A 46-year-old man had suffered from diabetes for five years and was admitted to the hospital with gangrene of the left foot. He had had exertional dyspnea for some time, but gave no definite history of myocardial infarction. Shortly after a surgical debridement, he was seized with severe retrosternal pain and dyspnea, went into shock, and died three hours later. No cardiac glycosides were given.

Electrocardiographic Findings.—An electrocardiogram obtained one hour after the onset of the shock is reproduced in Fig. 18,*D*. The QRS pattern was essentially the same as that in a preoperative tracing which is not reproduced. The initial deflection was upright in all precordial leads. The R wave was unusually small in Leads V_2 and V_3, and when taken in conjunction with the subsequent deep S wave, was attributable to left ventricular hypertrophy. The QRS complexes in left ventricular Leads V_4 through V_6 and aV_F were in no way suggestive of infarction. On the other hand, Lead aV_L displayed a QR complex, a slight elevation and bowing of the RS-T segment, and inversion of the T wave, suggestive of lateral infarction. This Q wave was cancelled out from Lead I because of a greater early negativity of the right arm, which was recorded as an upright deflection in Lead I. The slurring of the Q wave in aV_L and the time interval of 0.03 second from its onset to nadir constituted further evidence strongly in favor of infarction. However, it was necessary to consider vertical position with transmission of cavity potentials through the mitral orifice and atrium to the left arm as an alternative explanation for the QRS-T pattern in Lead aV_L. The fact that the P wave in Lead aV_L was isoelectric gave no help in the differentiation and left the source of the QRS-T pattern in doubt. For this reason, an unequivocal diagnosis of lateral infarction was not justified. High precordial and axillary leads were indicated, but were not obtained in this case. The preoperative tracing showed isoelectric RS-T junctions in Leads V_4 through V_6 and aV_F and a localized inversion of the T wave in Lead V_4, whereas the postoperative tracing revealed RS-T depression in Leads V_4, V_5, and aV_F and reversal in the direction of the T wave in V_4. The RS-T depression was strongly suggestive of acute left ventricular ischemia, secondary to the shock. A change from an inverted to an upright T wave is the reverse of the usual finding in ischemia, but has been observed during induced angina pectoris.[16] However, no significant change took place in the QRS-T pattern in Lead aV_L, indicating that the lateral infarct, if present, had occurred prior to hospitalization.

Pathologic Findings.—The heart weighed 358 grams and exhibited an aneurysm of the basal two-thirds of the lateral wall, secondary to an old, healed infarction, involving the entire lateral wall, and continuing slightly into the anterior and posterior walls, as demarcated by the area of avascularity in the roentgenogram (Fig. 20). Because of the size of the infarct, QRS abnormalities should have been recorded in Leads V_6 and aV_F as well as in aV_L. Microscopic blocks showed no evidence of recent infarction, but did not exclude terminal damage to the subendocardial portion of the anterolateral wall, since the three-hour interval between the onset of shock and death may have been too short for the development of histologic changes.

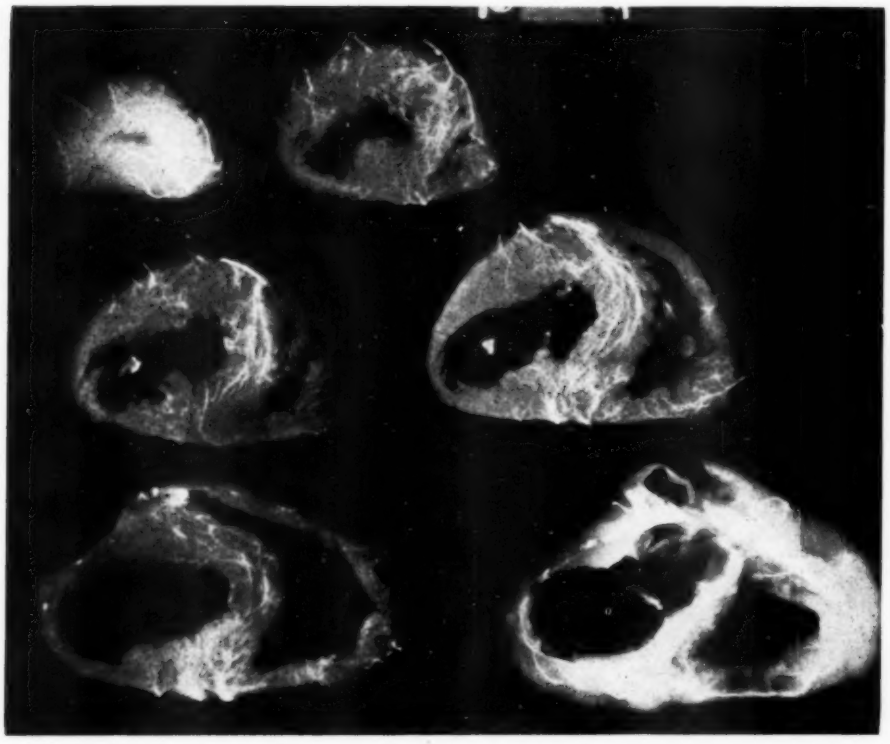

Fig. 20.—Roentgenogram of the injected heart in Case 158 with a large, healed lateral infarct demarcated by the avascularity and thinning of the wall.

CASE 159.—An 84-year-old woman was brought to the hospital in coma with marked peripheral circulatory collapse, an apical heart rate of 190 per minute, and signs of occlusion of the left brachial artery. Past history was unobtainable. Death occurred on the third hospital day.

Electrocardiographic Findings.—An electrocardiogram obtained on the first hospital day revealed auricular flutter with a 2:1 ventricular response and right bundle branch block. The findings were typical of right bundle branch block in all leads except aV_L, which displayed an initial Q wave 0.03 second in duration followed by a slurred R wave. In a tracing made on the following day after the administration of 0.8 mg. of Cedilanid, auricular fibrillation had replaced flutter and the right bundle branch block had disappeared. The initial deflection was upright in all precordial leads and the QRS complexes in these leads were not remarkable in contour. In Lead aV_L the QR complex was still present and consisted of a Q wave 0.03 second in duration, 2.0 mm. in depth, and 40 per cent of the succeeding R wave. The consistently abnormal QR complex in aV_L was strongly suggestive of high lateral infarction, but the possibility of its transmission from the left ventricular cavity through the mitral orifice could not be positively excluded. The initial Q wave was obliterated in Lead I because of greater initial negativity of the right than the left arm.

Pathologic Findings.—The heart weighed 500 grams and revealed an old, completely healed and partially calcified subendocardial infarct involving the lateral wall at the base and extending backward into the posterolateral wall near the apex. The position of this infarct corresponded closely with that in Case 145 (Fig. 9), except that the involvement of the second segment of this case was comparable to that of the third segment of Fig. 9. The lesion was confined to the subendocardial one-half of the wall and showed no evidence of recent activity. This infarct ex-

plained adequately the abnormal QR pattern in Lead aV_L. The absence of diagnostic signs in Leads V_6 and V_5 was probably due to the fact that the infarct had not reached the apical segment and was confined to a small portion of the posterolateral wall in the second and third segments. Involvement of the posterolateral wall was not evident in Lead aV_F, presumably because the heart was in horizontal position.

CASE 160.—A 52-year-old man gave a history of abrupt congestive failure four years previously with complete recovery. He was able to carry on normal activity until one month before hospital admission, when there was recurrence of paroxysmal nocturnal dyspnea followed by progressive edema. Thoracic pain was denied. He had been taking digitalis under the direction of his family physician, but was in advanced congestive heart failure on admission and failed to respond to therapy, expiring on the fourth day.

Electrocardiographic Findings.—An electrocardiogram obtained one hour after admission is reproduced in Fig. 18,*E*. Auricular fibrillation was present. The similarity of the RS complex in V_2, V_3, and V_4 to that in Lead V_1 indicated that all four leads were reflecting the potential variations of the right ventricle, as a result of either right ventricular dilatation or of displacement of the heart to the left. In Lead V_5, there was a barely detectable initial R wave followed by an S wave, which was notched near its termination, and in Lead V_6 there was a small, notched R wave and inverted T wave. The findings in Lead V_5 were suggestive of a small, patchy, anterolateral infarct, but might have represented a transitional zone phenomenon in a case of right ventricular dilatation. The equiphasic QR complex of aV_L was also suggestive of lateral infarction. Transmission from the posterobasal, rather than the lateral wall of the left ventricle had to be considered in the differential diagnosis, but reference of cavity potentials through the mitral orifice to the left arm could be excluded because the heart was in semihorizontal to horizontal position. From the RST-T pattern, it was believed that the patchy infarct of the anterolateral wall was old and healed.

Pathologic Findings.—The heart weighed 523 grams and exhibited both left ventricular hypertrophy and right ventricular dilatation and hypertrophy. A small, completely healed infarct was found in the subendocardial one-half of the anterolateral wall in the two apical segments and was comparable in size and position to the lesion in the two apical segments in Case 146 (Fig. 11). Although there was correspondence between the findings in Leads V_5 and aV_L and the position of the infarct at autopsy, there was uncertainty as to whether the findings in V_5 were the result of the infarct or merely a transitional zonal phenomenon.

CASE 161.—An 81-year-old diabetic man had suffered from angina pectoris for three years and from intermittent claudication for five weeks. He was admitted to the hospital because of gangrene of the left leg. Amputation was performed, but death occurred on the fifth hospital day.

Electrocardiographic Findings.—An electrocardiogram obtained twenty-four hours after admission is reproduced in Fig. 18,*F*. The QRS-T complex was considered to be within normal limits in all precordial leads. The heart was in horizontal position and the T waves in Lead aV_L and Lead I were isoelectric, but the limb leads also showed no evidence of infarction.

Pathologic Findings.—The heart weighed 379 grams and exhibited a small, completely healed, patchy infarct, confined to the subendocardial one-half of the lateral wall in the apical three segments and comparable in size and position to the infarct in the corresponding segments in Case 146 (Fig. 11). There was no evidence of recent involvement. This case illustrates the fact that an infarct confined to the subendocardial portion of the lateral wall may be completely missed in the six precordial leads and in the standard and unipolar extremity leads. A clinical history of coronary disease without specific abnormalities in the routine electrocardiogram constitutes an indication for additional high axillary and precordial leads and for esophageal leads.

COMMENT

The criteria for the interpretation of the findings in Leads V_5, V_6, and aV_L have been covered in detail,[3] and the electrocardiographic patterns associated with anterolateral infarction and those of posterolateral infarction have been described in previous reports.[4,5] The correlation between electrocardiographic and pathologic findings in primary lateral infarction has been considered in individual case reports, but remains for summary. The twenty-seven cases have been classified into three groups according to the distribution of the lesion at autopsy: (A) infarction of the basal one-half of the lateral wall, continuing for a variable distance into the apical one-half (fourteen cases); (B) infarction involving chiefly the apical one-third of the lateral wall (eleven cases); and (C) infarction confined to the mid-portion of the lateral wall (two cases).

Correlation of Electrocardiographic and Pathologic Findings in Group A.— The common pathologic finding which led to the classification of fourteen cases into this group was infarction of the greater portion of the basal one-half of the lateral wall of the left ventricle and the variable features necessitating further subdivision were referable to the involvement of the apical one-half of the lateral wall, the distribution between endocardium and epicardium, and the age of the lesion. Most of these infarcts were shaped like a bullet. The base lay high in the lateral wall parallel to the atrioventricular groove, but generally separated from it by a narrow strip of intact myocardium, whereas the blunted apex usually projected into the apical one-third of the left ventricle. In three patients (Cases 144, 147, and 153) the long axis of the infarct was parallel to that of the left ventricle and the lesion spared the apical one-third or more of the lateral wall. In seven patients the infarct ran diagonally backward, terminating in the apical one-third of the posterolateral wall in five (Cases 142, 145, 152, 154, and 159), but reaching the tip of the posterolateral wall in two (Cases 151 and 158). In four patients the infarct ran diagonally forward, terminating in the apical one-third of the anterolateral wall in one (Case 143), but reaching its tip in three (Cases 146, 148, and 150). The infarct was transmural throughout in three patients (Cases 148, 151, and 158); transmural in its basal and subendocardial in its apical portion in two (Cases 142 and 146); confined to the subepicardial one-fourth of the wall in one (Case 150), and to the subendocardial one-half in the other eight patients. Electrocardiographic studies were available during the acute stage in nine patients, after healing in four (Cases 145, 154, 158, and 159), and during both stages in one (Case 151).

The lesion limited to the subepicardial layer in Case 150 was manifested by normal QRS complexes and deeply inverted T waves in leads from the left side of the precordium. The electrocardiographic findings were typical of pericarditis and thus conformed closely with the pathologic findings.

In the remaining thirteen patients, the infarct involved the subendocardial layer of most of the basal one-half and at least a portion of the apical one-half of the lateral wall and should have been manifested by an abnormal Q-wave pattern in overlying leads. However, no Q waves were recorded in either Lead

V_5 or V_6 in six patients; relatively small Q and tall R waves more in keeping with left ventricular hypertrophy were found in three; and abnormal Q waves were present in one or both leads in only four (Cases 142, 151, 152, and 153). The Q waves in Leads V_5 and V_6 in Cases 152 and 153 were attributable exclusively to a separate healed infarct of the anterolateral aspect of the apex found at autopsy, since they were present in tracings taken two months before the advent of the large, terminal lateral infarct and were unchanged in tracings taken subsequent to its development. Moreover, the fact that serial tracings in Case 142 showed no changes in the QRS-T pattern in Leads V_5 and V_6 suggested that the abnormalities in these leads were due to the healed anteroapical infarct found at autopsy rather than to the recent extensive lateral infarct. This left only one patient (Case 151) in whom an abnormal Q wave in Lead V_6 was referable to primary high lateral infarction. Even in this case, however, the QR complex in Lead V_6 was considered diagnostic only in the first tracing, taken soon after the development of the lesion, and could merely be regarded as suspicious of lateral infarction in subsequent tracings taken after healing.

The rarity of abnormal Q waves in Leads V_5 and V_6 in association with infarction involving most of the basal one-half of the lateral wall and extending into a portion of the apical one-half stands in striking contrast to our previous demonstration of abnormal Q waves in one or both of these leads in fifty of fifty-seven patients with evidence of pathologic infarction involving the apical one-third or more of the anterior and lateral walls of the left ventricle.[4] These Q waves could be correlated with infarction of the apical one-third of the anterolateral and lateral walls, since lesions limited to the anteroseptal portion of the apex did not produce abnormal Q waves in Leads V_5 and V_6 unless there was marked clockwise rotation of the heart.[17] The lack of diagnostic Q-wave patterns in Leads V_5 and V_6 was probably due to the tendency of high lateral infarcts to spare the apical one-third of the anterolateral wall. The lesion extended through the anterolateral wall to reach its tip in only two of the thirteen patients (Cases 146 and 148). The registration of initial R, rather than Q waves in Leads V_5 and V_6 of both patients may have been due to the short interval between the onset of the infarcts and recording of the electrocardiograms.[4] However, the presence of Q waves in more medial leads in the latter case suggested an additional factor which will be discussed.

QRS-T abnormalities sufficient to arouse the suspicion of anteroseptal infarction or to lead to its ante-mortem diagnosis were found in one or more of the first four precordial leads in five patients (Cases 143, 144, 146, 147, and 148) in which autopsy revealed infarction of the lateral or anterolateral wall, but not of the septum nor adjoining anterior wall. Despite the absence of histologic changes in the anteroseptal wall in Case 146, the occlusion near the mouth of the anterior descending coronary artery suggested that sufficient anteroseptal ischemia might have been present to have accounted for the marked RS-T depression, with normal initial R waves in Leads V_1 through V_4. A comparable RS-T depression in the same leads in Case 148 was associated with absence of the R wave from these leads and hence was not explained fully by the hypothesis of a histologically unrecognizable anteroseptal ischemia. It is possible that the

abnormalities in Leads V_1 through V_4 were due to precordial transmission of the potential variations of the large infarct of the anterolateral and lateral walls. The acutely inverted T waves in Leads V_2 and V_3 of the tracing of June 4, 1946, in Case 151 probably reflected the altered repolarization of an ischemic zone beyond the border of the high anterolateral infarct subsequently demonstrated at autopsy.

More decisive evidence of the transmission of the potential variations of the basal portion of the lateral wall to the precordium was obtained in Case 144. A QR pattern diagnostic of infarction was found localized to precordial Positions 3 and 4, not only in the customary precordial leads, but also in those taken at the level of the third intercostal space. The Q wave was much deeper and the Q/R ratio much greater in the high than in the low chest leads. In the antemortem interpretation, these findings were attributed to a subendocardial anteroseptal infarct, maximal at the base and diminishing toward the apex, but at autopsy the infarct was localized to the subendocardial portion of the basal one-half of the lateral wall and did not extend into the anterior wall. Transmission of the potential variations of the epicardial surface of the lateral wall to the precordium was apparently facilitated in this case by marked counterclockwise rotation of the heart. The combination of counterclockwise rotation and displacement of the transitional zone to the right in Case 143 may have permitted transmission of the potential variations of the infarcted basal portion of the anterolateral wall far enough to the right to explain the QR pattern in Leads V_1 and V_2. In Case 147 an abnormal QR complex was also recorded in Lead V_1 and a comparable lesion of the basal portion of the anterolateral wall was demonstrated at autopsy, but no evidence was found of the type of cardiac rotation present in Cases 143 and 144. Since no other cause for the QR pattern in V_1 was found, it was tentatively attributed to the infarct by the process of exclusion.

In one additional patient from Group B (Case 60), much deeper and broader Q waves were recorded in Leads V_3 and V_4 than in V_5 and V_6, despite the fact that the infarct involved the apical one-third of the lateral wall and only the apical 1.0 cm. of the anteroseptal wall. The lateral infarct was manifested by electrocardiographic signs of anteroseptal infarction in this case, as in Case 144, because of marked counterclockwise rotation which facilitated transmission of the potential variations of the lateral wall of the left ventricle to the precordium. The situation in these cases was opposite to that in Cases 67 and 68 where QS complexes in Leads V_5 and V_6 were attributable to the transmission of the potential variations of an infarcted anteroseptal wall to the axilla, as a result of marked clockwise rotation of the heart.

The findings in Lead aV_L were more distinctive than those in the precordial leads, QR patterns being recorded in aV_L in eleven of the thirteen cases. The minute, multiphasic QRS complex in one of the two remaining patients (Case 146) was probably transmitted from the epicardial surface covering the anterior end of the interventricular septum, as a result of clockwise rotation of the heart into a semivertical position. The initial R wave in Lead aV_L of the other patient (Case 148) was subject to the same explanation as its counter-

part in Lead V_6. The QR pattern in Lead aV_L was considered diagnostic of lateral infarction in Case 154 because of the notching and prolongation of the upstroke of the R wave, and in Case 152 because of the nature of the change from preceding tracings; whereas the QR pattern in Cases 142, 145, 147, 158, and 159 was regarded as strongly suggestive, but not quite pathognomonic, either because of low voltage or because of an element of uncertainty as to its source. The QR pattern in Lead aV_L in Cases 143, 144, and 151 was suspicious of lateral infarction, but was more likely due to left ventricular hypertrophy, whereas that in Case 153 was also suggestive, but was of indeterminate significance because of associated right bundle branch block. In three of the seven patients with findings in Lead aV_L regarded as diagnostic or strongly suggestive of lateral infarction, Leads V_5 and V_6 displayed initial R waves, and in two others, Leads V_5 and V_6 showed QR deflections more in keeping with left ventricular hypertrophy. Thus, lateral infarction may be manifested by signs in Lead aV_L, but not in the customary precordial leads.

Standard Lead I was not an adequate substitute for Lead aV_L, since Lead I revealed an initial upstroke in five of the eleven patients with QR patterns in aV_L which were either diagnostic, strongly suggestive, or suspicious of infarction. The reason for this discrepancy is that Lead I records the potential differences of the two upper extremities, whereas Lead aV_L records chiefly the potential variations of the left arm. A Q wave in Lead aV_L was not carried over into Lead I when there was greater early negativity in the right than the left arm, as evidenced by a deeper initial downstroke in Lead aV_R than in aV_L.

From this small series of cases of high lateral infarction, it would appear that Lead aV_L usually yields signs which are at least suspicious of the lesion, but seldom furnishes evidence which may be regarded as pathognomonic. The presence of signs suggestive of infarction in the customary precordial or left arm leads, as emphasized by the Wilson group,[13,14] constitutes an indication for supplementary leads higher in the precordium and axilla. The same criteria were used tentatively for the interpretation of the findings in high precordial and axillary leads taken at the horizontal level of the sternal terminus of the third intercostal space as for the corresponding official precordial lead located in the same vertical plane. However, a revision may be necessary upon completion of a current study of normal variations in the findings in these leads.

The value of high precordial leads is well illustrated by Case 145. The customary precordial leads in this case yielded evidence which was regarded as only slightly suspicious of infarction, whereas Lead aV_L displayed a QR complex that was strongly suggestive, but not diagnostic, of lateral infarction. The demonstration of an abnormal QR complex localized to a lead from the anterior axillary line at the level of the third intercostal space was considered diagnostic of high lateral infarction and was subsequently correlated with a lesion of the subendocardial one-half of the lateral wall at autopsy. An abnormal QR complex was recorded in a lead high in the mid-axilla in Case 151 after diagnostic signs had disappeared from tracings at the sixth precordial position. This conformed with the pathologic findings of more extensive infarction in the basal than in the apical one-half of the lateral wall. More marked QR abnormalities

in high than in the customary precordial leads in Case 144 could be correlated with a lesion limited to the basal one-half of the wall. The opposite finding of more marked QR abnormalities in V_5 and V_6 than in high axillary leads was encountered in Case 46 and corresponded with infarction which involved chiefly the apical one-half of the lateral wall at autopsy.

The experience with high precordial leads in the foregoing cases and in a larger group that did not come to autopsy has warranted a more extensive study to determine their value and limitations in the detection of high anterior and lateral infarcts and in the delineation of the upper boundaries of apical infarcts. Accordingly, leads at the intersection of a horizontal line through the sternal terminus of the third intercostal space with lines in the vertical plane of precordial Positions 3, 4, 5, and 6 are now being taken routinely in this clinic along with Leads V_1 through V_6.

Correlation of Electrocardiographic and Pathologic Findings in Group B.— The common pathologic finding which led to the classification of eleven patients into this group was infarction of the apical one-third of the lateral wall. The lesion was large in two patients, involving the apical two-thirds of the lateral wall in Case 141 and the apical one-half to two-thirds of the lateral and posterolateral walls in Case 157. The involvement of the lateral wall was limited to the apical one-third or, at the most, to the apical one-half in the remaining nine patients (Cases 17, 60, 138, 139, 140, 155, 156, 160, and 161). In Case 17 the infarct covered the apical one-third of the anterolateral and anteroseptal walls; in Cases 60, 138, 139, 140, and 155 the lesion occupied the apical one-third of the lateral wall, but continued into the anteroseptal portion of the extreme apex; in the remainder it was confined to the lateral wall. The infarct was transmural in Case 141, in part transmural and in part subendocardial in Case 17, dense in the subendocardial one-half and patchy in the outer one-half in Cases 60, 139, and 157, subendocardial to mid-zonal in Cases 138 and 140, and confined to the subendocardial one-half in the remainder. Electrocardiographic studies were available during the acute stage in four of the patients (Cases 60, 138, 139, and 140) and only after healing in the other five.

Abnormal Q waves diagnostic of infarction were present in Lead V_5 or in both V_5 and V_6 in five patients (Cases 17, 60, 139, 141, and 155), and QRS changes somewhat suggestive of infarction were found in these leads in three others (Cases 156, 157, and 160). Lead aV_L also showed a QR complex diagnostic of infarction in Cases 17, 141, and 155, and QRS changes strongly suggestive of infarction in Cases 60, 156, 157, and 160. Thus, QR patterns diagnostic, or at least strongly suggestive, of infarction were present in Leads V_5, V_6, and/or aV_L in eight of the eleven patients with infarction of the apical one-third of the lateral wall. On the other hand, in Case 161 there were no signs in the electrocardiogram to arouse the suspicion of the healed, patchy, subendocardial infarct found at autopsy in the apical one-half of the lateral wall.

The electrocardiographic findings in the two remaining patients (Cases 138 and 140) conformed more or less to the pattern described by Wood, Wolferth, and Bellet.[8] The marked RS-T depression and T-wave inversion in Leads V_4, V_5, and V_6 of both patients corresponded closely with the pathologic dem-

onstration of acute infarction which occupied the subendocardial layer and mid-zone of the apical one-third of lateral and anterolateral walls, respectively, but spared the subepicardial layer throughout. The absence of abnormal Q waves from Leads V_4, V_5, and V_6 of both patients was explained by the fact that the lesion in the anterolateral and extreme anterior aspects of the apex was located principally in the mid-portion of the wall and spared enough of the subendocardial muscle so that the onset of activation was not delayed.

The first electrocardiogram in Case 139, taken four and one-half hours after the onset of the pain, showed normal R waves and marked RS-T depression in Leads V_4, V_5, and V_6, whereas a second electrocardiogram, taken forty-four hours later, showed significant reduction in the initial R wave of V_4 and V_6 and a QR complex in Lead V_5 that conformed closely with the relatively small subendocardial anterolateral infarct found at autopsy. Thus, the pattern of Wood, Wolferth, and Bellet[8] may be observed as an early, but transient finding referable to acute ischemia or to early subendocardial infarction which has not progressed to the point of obliterating the response to the activating impulse.

Correlation of Electrocardiographic and Pathologic Findings in Group C.—A small, thin, subendocardial infarct confined to the middle one-third of the lateral wall was found in Cases 4 and 149. The electrocardiographic findings in both cases were consistent with the pattern of Wood and associates,[8] but those in Case 149 could have been due to a combination of left ventricular hypertrophy and digitalis action. The absence of Q waves from Leads V_5 and V_6 could be explained by the small size of the infarct and the probability that the potential variations of the overlying epicardium were referred higher in the axilla than precordial Positions 5 and 6. The fewer the number of precordial leads taken, the smaller the chance of placement of the electrode over the central or marginal zone of moderate sized infarcts. Thus, in patients with relatively small infarcts of the anterior or lateral aspects of the apex, the use of six precordial leads (V_1 through V_6) may uncover a localized abnormal Q wave diagnostic of the lesion, whereas the employment of only one or two leads may yield no signs or may show RS-T abnormalities without QRS changes. In patients with relatively small infarcts situated high in the anterior or lateral wall, supplementary high precordial or axillary leads may reveal diagnostic Q waves when the customary six precordial leads are unrevealing or show isolated RS-T abnormalities. Thus, the registration of patterns like that of Wood, Wolferth, and Bellet[8] should constitute an indication for additional exploratory leads in an effort to demonstrate QRS abnormalities more definitely diagnostic of infarction.

SUMMARY

Infarction of the lateral wall of the left ventricle was demonstrated pathologically in 105 cases, which represents an incidence of 65 per cent in a series of 161 cases. The cases of anterolateral infarction and those of posterolateral infarction have been analyzed in previous reports and the present study was concerned with a correlation of electrocardiographic and pathologic findings in twenty-seven cases of primary lateral infarction. These cases were classified into three groups,

according to the distribution of the lesion at autopsy: (A) high, (B) low, and (C) midlateral infarction.

A. High lateral infarction, involving chiefly the basal one-half of the lateral wall, but continuing for a variable distance into the apical one-half, was found in fourteen cases. The infarct was limited to the subepicardial layer in one case and was manifested by normal QRS complexes and deeply inverted T waves typical of the findings in pericarditis. Despite the fact that the high lateral infarct was transmural in five cases and subendocardial in the other eight, it was manifested by a diagnostic QR pattern in Lead V_5 or V_6 in only one case. The rarity of abnormal Q waves in Leads V_5 and V_6 of this group contrasted sharply with their frequency in association with infarction of the apical one-third of the anterolateral wall and was ascribed to the fact that high lateral infarcts generally spared most or all of the apical one-third of the anterolateral wall. On the other hand, Lead aV_L yielded a QR pattern which was considered diagnostic of lateral infarction in two cases, strongly suggestive in five cases, and suspicious in four cases. Standard Lead I was not an adequate substitute for Lead aV_L because it failed to show an initial downstroke in five of the eleven patients with Q waves in aV_L, because of greater initial negativity of the right than the left arm. Signs suggestive of infarction in the customary precordial or left arm leads constitute an indication for exploration of the upper precordium and axilla. Leads at the intersection of a horizontal line through the sternal terminus of the third intercostal space with vertical lines in the plane of precordial Positions 3, 4, 5, and 6 were obtained on four patients who were followed to autopsy. In one case, the findings in the customary precordial leads were equivocal, those in Lead aV_L were strongly suggestive, but those in the high precordial leads were pathognomonic of the high lateral infarct found at autopsy. The findings in the high precordial leads taken in conjunction with those in the customary leads in the other three cases aided in establishing the diagnosis and in localizing the position of the infarct.

B. Low lateral infarction was found in eleven cases and was largely or entirely confined to the apical one-third of the lateral wall in eight of these. Abnormal Q waves diagnostic of infarction were present in Lead V_5, V_6, and/or aV_L in five cases, and strongly suggestive QR patterns were found in three others. The electrocardiogram was negative in one case and conformed to the pattern of Wood, Wolferth, and Bellet in the other two cases. The RS-T depression in V_4, V_5, and V_6 could be correlated with acute infarction which involved the subendocardial and mid-zones, but spared the subepicardial layer, and the absence of Q waves was explained by the patchy character of the subendocardial lesion. A similar pattern was recorded in an electrocardiogram taken four and one-half hours after the onset of the pain in one other case, but was subsequently replaced by a QR complex diagnostic of the subendocardial infarct found at autopsy.

C. Small mid-lateral infarcts, involving the subendocardial layer of the middle one-third of the lateral wall, were found in two cases. A pattern resembling that of Wood, Wolferth, and Bellet was found in both cases, but could have been produced by a combination of left ventricular hypertrophy and

digitalis action in one of these. The absence of Q waves may have been due to the small size of the lesion and the failure to take high axillary leads.

QRS-T abnormalities in one or more of the first four precordial leads, which were suggestive of anteroseptal infarction, but were actually a manifestation of the lateral infarction, were found in five cases. Transmission of the potential variations of the infarcted lateral wall to the precordium was facilitated by marked counterclockwise rotation in three of these cases. This situation was the opposite of that in previously reported cases where abnormal Q waves were recorded in Leads V_5 and V_6 as a result of clockwise rotation sufficient to cause reference of the potential variations of an infarcted anteroseptal wall to the axilla.

REFERENCES

1. Wilson, F. N., Johnston, F. D., Rosenbaum, F. F., Erlanger, H., Kossmann, C. E., Hecht, H., Cotrim, N., de Oliveira, R. M., Scarsi, R., and Barker, P. S.: Precordial Electrocardiogram, Am. Heart J. **27**:19, 1944.
2. Wilson, F. N., Rosenbaum, F. F., and Johnston, F. D.: Interpretation of the Ventricular Complex of the Electrocardiogram, Advances in Internal Medicine, **2**:1, 1947, Interscience Publishers, New York.
3. Hecht, H. H.: The Localization of Myocardial Infarcts With Particular Reference to Lateral Infarction and to the T_1Q_3 Pattern, Proc. Am. Federation Clin. Research **2**:102, 1945.
4. Myers, G. B., Klein, H. A., and Hiratzka, T.: Correlation of Electrocardiographic and Pathologic Findings in Large Anterolateral Infarcts, Am. Heart J. **36**:838, 1948.
5. Myers, G. B., Klein, H. A., and Hiratzka, T.: Correlation of Electrocardiographic and Pathologic Findings in Posterolateral Infarction, Am. Heart J. (In press.)
6. Myers, G. B., and Oren, B. G.: The Use of the Augmented Unipolar Left Leg Lead in the Differentiation of the Normal From Abnormal Q Waves in Standard Lead III, Am. Heart J. **29**:708, 1945.
7. Myers, G. B., Klein, H. A., and Hiratzka, T.: Correlation of Electrocardiographic and Pathologic Findings in Posterior Infarction, Am. Heart J. (In press.)
8. Wood, F. C., Wolferth, C. C., and Bellet, S.: Infarction of the Lateral Wall of the Left Ventricle; Electrocardiographic Characteristics, Am. Heart J. **16**:387, 1938.
9. Thomson, H. W., and Feil, H.: Infarction of the Lateral Wall of the Left Ventricle, Am. J. M. Sc. **207**:588, 1944.
10. Shaffer, C. F.: Electrocardiographic Study of Lateral Infarction, Proved at Autopsy, Am. Heart J. **28**:39, 1944.
11. Goldberger, E.: The Differentiation of Normal From Abnormal Q Waves, Am. Heart J. **30**:341, 1945.
12. Myers, G. B., and Klein, H. A.: The Relation of Unipolar Limb Leads to Precordial and Esophageal Leads, Am. Heart J. **35**:727, 1948.
13. Rosenbaum, F. F., Wilson, F. N., and Johnston, F. D.: The Precordial Electrocardiogram in High Lateral Myocardial Infarction, Am. Heart J. **32**:135, 1946.
14. Wilson, F. N., Johnston, F. D., Rosenbaum, F. F., and Barker, P. S.: On Einthoven's Triangle, the Theory of Unipolar Electrocardiographic Leads, and the Interpretation of the Precordial Electrocardiogram, Am. Heart J. **32**:277, 1946.
15. Myers, G. B., Klein, H. A., and Stofer, B. E.: The Electrocardiographic Diagnosis of Right Ventricular Hypertrophy, Am. Heart J. **35**:1, 1948.
16. Parade, G. W.: Aufrichtung der coronaren T-Zacke nach körperlicher Anstrengung, Klin. Wchnschr. **13**:1791, 1934.
17. Myers, G. B., Klein, H. A., and Stofer, B. E.: Correlation of Electrocardiographic and Pathologic Findings in Anteroseptal Infarction, Am. Heart J. **36**:535, 1948.

EFFECT OF POTASSIUM ON DOWNWARD T WAVES OF PRECORDIAL LEADS OF NORMAL CHILDREN

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DOWNWARD T waves occur normally in the precordial leads of children.[1,2,3] In a previous paper[3] we pointed out that these downward T waves were limited to precordial leads which showed an RS pattern. In this paper, we shall describe the mechanism probably responsible for these downward T waves.

MATERIAL AND METHOD

Ten normal white and Negro children were studied. These were selected by the following process of elimination. Multiple precordial leads were taken at random on children from the surgical ward of Lincoln Hospital. The children were convalescing from traumatic conditions, such as fractures, and from minor surgical procedures. Their ages ranged from 3½ to 12½ years. Only those children who showed downward T waves in more than one precordial lead were used in this study.

In all cases the three standard leads, the three augmented unipolar extremity leads,[4] and six unipolar precordial leads[4,5] were taken. Tracings were taken before and one hour after the child drank a solution containing 5.0 Gm. of potassium salts. The solution contained equal amounts of potassium acetate, potassium bicarbonate, and potassium citrate. One dram of solution contained 1.0 Gm. of the salts.

RESULTS

Figs. 1, 2, and 3 show typical changes in the precordial leads which were produced by potassium. It is to be noted that all of the downward T waves became upward in the precordial leads of Figs. 2 and 3 and in all of the precordial leads except V_1 in Fig. 1. A downward T in Lead V_1, however, is not abnormal, even in adults.

One child showed downward T waves in precordial Leads V_1, V_2, V_3, V_4, and V_5 in the control tracings (Fig. 1). In this case, potassium caused the T waves to become upward in all these precordial leads except V_1.

One child showed downward T waves in Leads V_1, V_2, V_3, and V_4 in the control tracings (Fig. 4). Potassium caused the T wave in Lead V_4 to become

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upright; the T wave in Lead V_3 became biphasic and in Leads V_1 and V_2 the T waves became more downward. This apparently paradoxical effect of potassium is explained in the discussion.

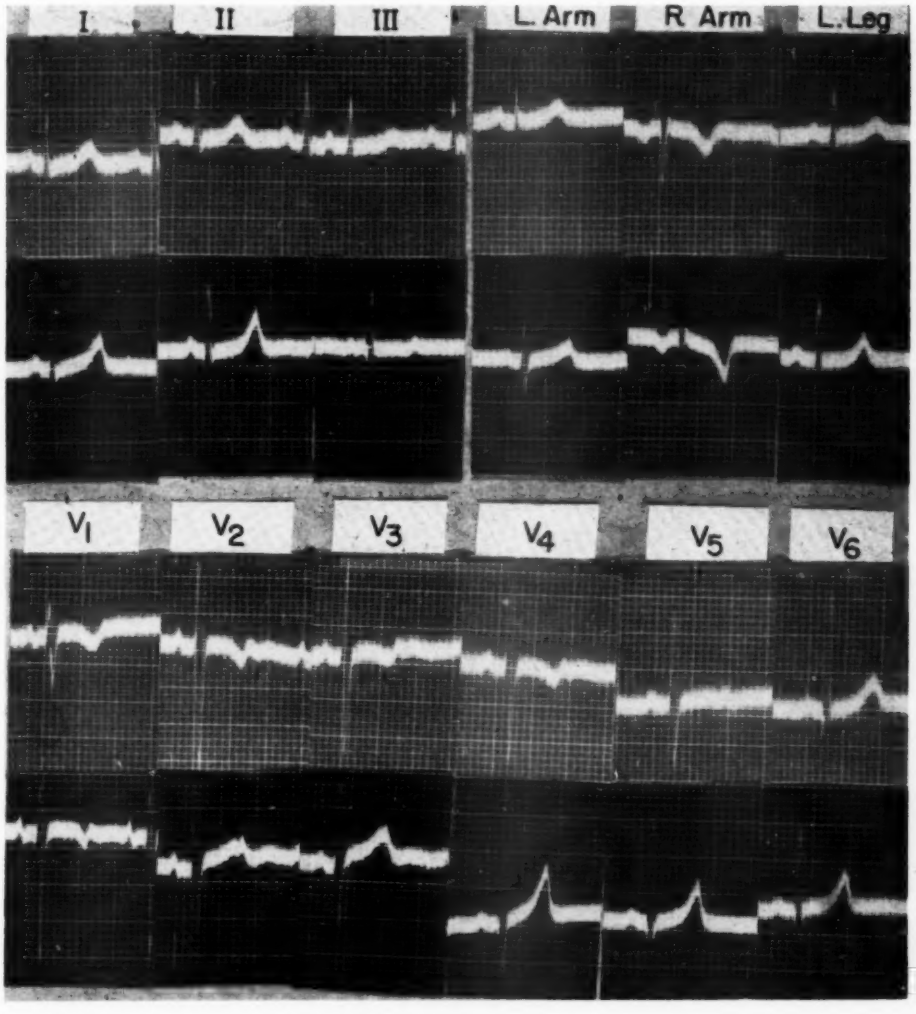

Fig. 1.—Tracings of a normal 5½-year-old white girl. Upper rows, control tracings. Lower rows, tracings taken one hour after the child drank a solution containing 5.0 Gm. of potassium salts.

Four children showed downward T waves in Leads V_1, V_2, and V_3 in the control tracings. Potassium caused the T waves to become upright in Leads V_2 and V_3 in three patients. In one child, a 12½-year-old boy, the T waves remained downward but became smaller.

Four children showed downward T waves in Leads V_1 and V_2 in the control tracings (Figs. 2 and 3). Potassium caused the T waves to become upright in

both leads in two cases and caused the T wave in Lead V_2 to become upright in two cases.

Potassium not only tended to make downward T waves in precordial leads become upright, but it also tended to make the upward T waves become taller and show a sharp peak (Figs. 1, 2, 3, and 4).

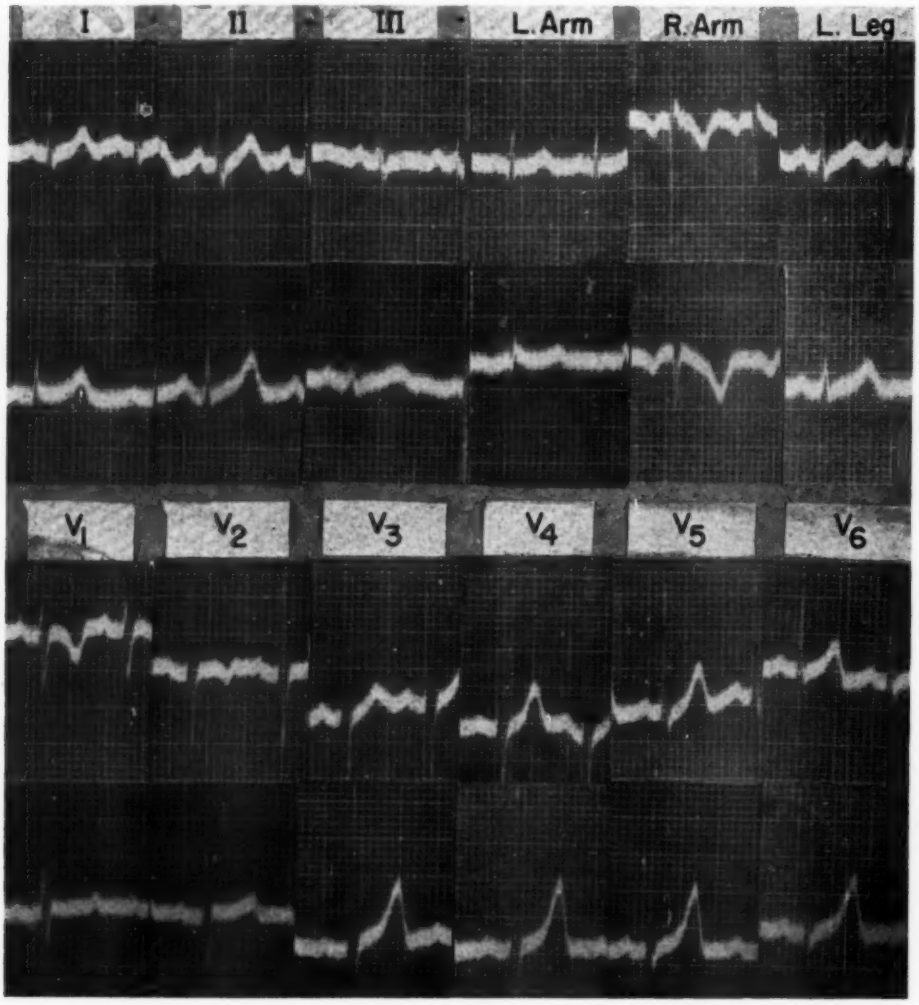

Fig. 2.—Tracings of a normal 9-year-old white girl. See legend of Fig. 1.

Other Electrocardiographic Changes.—In the unipolar extremity leads and standard leads, the direction of T did not change after potassium, but downward T waves usually became deeper and peaked, and upward T waves became taller and peaked (Figs. 1, 2, 3, and 4).

Potassium caused no significant changes in the P waves, P-R intervals, QRS complexes, Q-T intervals, and RS-T segments.

DISCUSSION

It is well known that the administration of potassium salts tends to make the T waves tall and peaked in the standard leads.[6] Similarly, patients with diseases associated with high blood potassium levels show tall, peaked T waves.[7] When the blood potassium level is low, the T waves become low or even inverted.[8] In such cases, the administration of potassium salts causes the T waves to become upright.[9]

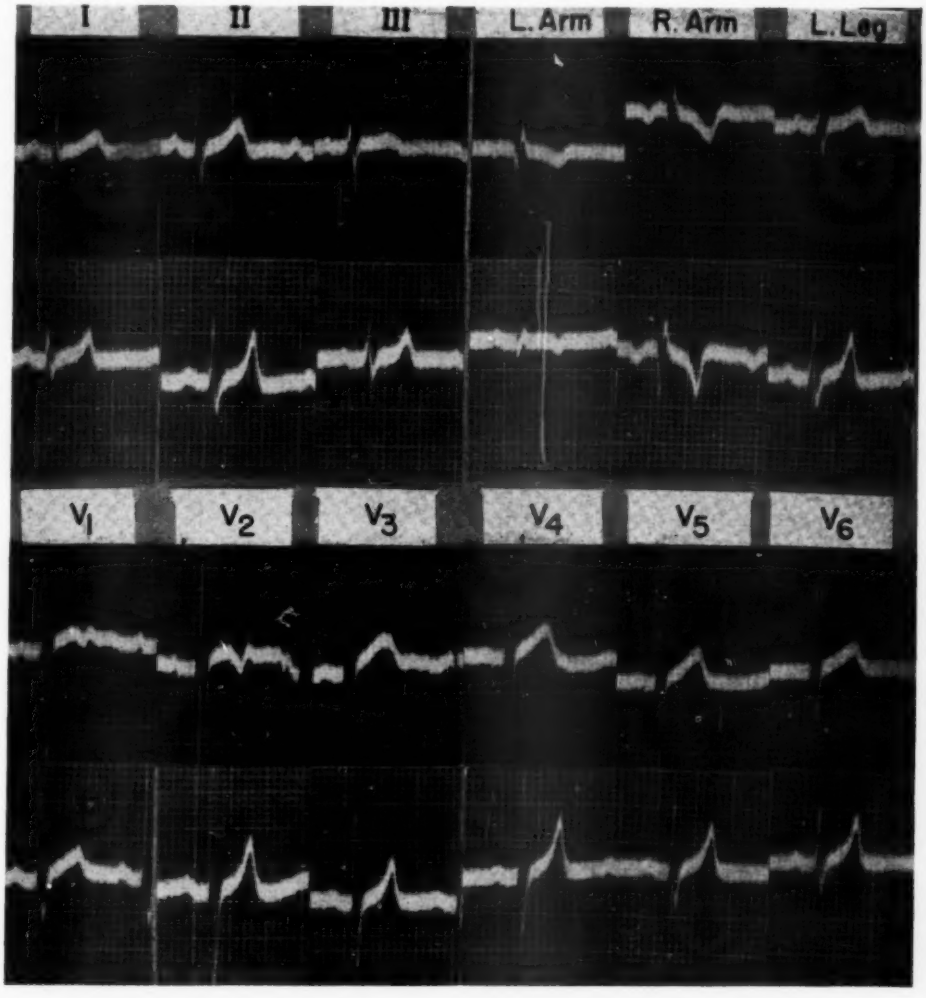

Fig. 3.—Tracings of a normal 4-year-old white boy. See legend of Fig. 1.

Our observations are of interest in that the downward T waves whose direction was reversed by potassium were localized to precordial leads. In this connection we can analyze the unusual effects of potassium shown in Fig. 4. It has been pointed out elsewhere[10] that the pattern of a unipolar lead depends

upon the surface of the heart which the lead faces. Unipolar precordial leads usually face either the epicardial surface of the right ventricle or the epicardial surface of the left ventricle. A unipolar precordial lead that faces the epicardial surface of the right ventricle shows an RS pattern with an upright or inverted T wave.[3,10] A unipolar precordial lead that faces the epicardial surface of the left ventricle shows a qR pattern and an upward T. Thus, the downward T

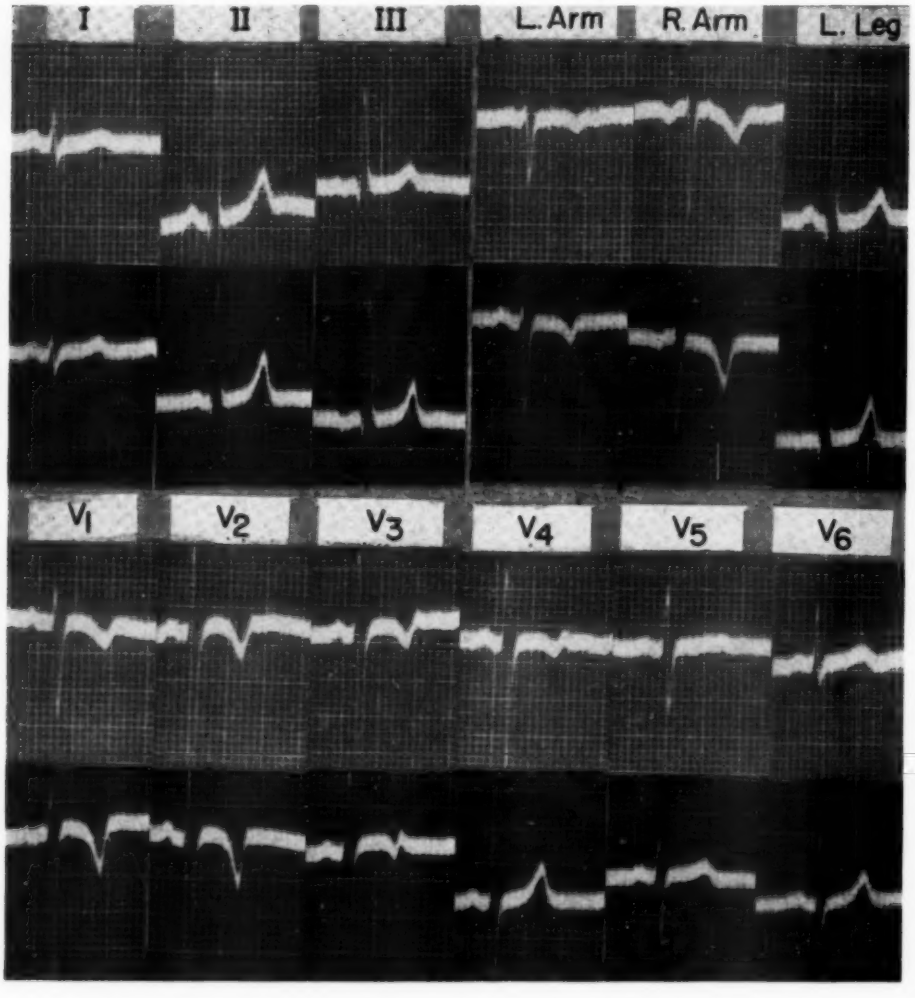

Fig. 4.—Tracings of a normal 11-year-old white boy. See legend of Fig. 1.

waves of the precordial leads of children are found in leads over the right ventricle.[3] However, the wall of the right ventricle barely extends beyond the right border of the sternum. Thus, Lead V_1 which is taken with the electrode to the right of the sternum tends to overlie the right auricle and face the cavity of the right ventricle. Leads that face the cavity of the right ventricle show an RS pattern and a downward T wave. Normally the unipolar right arm lead faces

the right ventricular cavity. Potassium in all our cases caused the T in the right arm lead to become deeper (Figs. 1, 2, 3, and 4). Therefore, if a precordial lead near the sternum were to face the cavity of the right ventricle rather than the epicardial surface of the right ventricle, T should become deeper after the administration of potassium. If clockwise rotation of the heart around its long axis were also present, the right ventricle would move toward the left and precordial Lead V_2 would also tend to face the right ventricular cavity in addition to Lead V_1.

Thus, in Fig. 4, if we assume that clockwise rotation of the heart around its long axis is present, Leads V_1 and V_2 would face the cavity of the right ventricle, just as the unipolar right arm lead does, and potassium should cause the T waves of all these leads to become deeper. This does occur. Evidence that clockwise rotation of the heart in Fig. 4 exists consists of the fact that precordial Lead V_6, which ordinarily faces the epicardial surface of the left ventricle, shows an RS pattern, indicating that it is facing the epicardial surface of the right ventricle because of clockwise rotation.[10,11]

This observation also helps to explain the fact that in eight of our ten cases, the downward T wave of Lead V_1 remained downward after potassium. However, in only two cases did the T wave in Lead V_1 become deeper; in six cases it became smaller. Possibly if we had given a larger dose of potassium in these six cases, the T would have become upward in Lead V_1 just as it did in Fig. 3.

The effect of potassium in reversing the downward T waves of precordial leads that face the epicardial surface of the right ventricle in children suggests that these downward T waves may be due to the fact that the right ventricular muscle contains less potassium than the muscle of the left ventricle. Exact proof of this by means of chemical analysis is, however, extremely difficult, if not impossible.

CONCLUSIONS

Normal children frequently show downward T waves in precordial leads which are taken near the sternum and which show an RS pattern. These downward T waves occur in leads that face the right ventricular cavity or the epicardial surface of the right ventricle. The administration of potassium salts causes the downward T waves of precordial leads that face the epicardial surface of the right ventricle to become upright. The T waves of precordial leads that face the cavity of the heart, such as Lead V_1 and rarely Lead V_2, may become deeper after potassium. Potassium makes upward T waves in precordial leads taller and peaked. In the unipolar extremity leads and standard leads, potassium does not change the direction of the T waves but makes upward T waves taller and peaked and downward T waves deeper and peaked.

ADDENDUM

Normal Negro adults frequently show downward T waves in precordial leads, similar to children. We have been able to cause these T waves to become upward by the administration of 10 Gm. of potassium salts. These observations will be reported elsewhere in detail.

REFERENCES

1. Master, A. M., Dack, S., and Jaffe, H. L.: Chest Leads in Normal Children, Proc. Soc. Exper. Biol. & Med. **32**:1529, 1935.
2. Robinow, M., Katz, L. N., and Bohning, A.: The Appearance of the T Wave in Lead IV in Normal Children and in Children With Rheumatic Heart Disease, AM. HEART J. **12**:88, 1936.
3. Goldberger, Emanuel: Significance of Downward T Waves in Precordial Leads of Normal Children, Am. J. Dis. Child. **71**:618, 1946.
4. Goldberger, Emanuel: A Simple Electrocardiographic Electrode of Zero Potential and a Method of Obtaining Augmented Unipolar Extremity Leads, AM. HEART J. **23**:483, 1942.
5. American Heart Association: Standardization of Precordial Leads, AM. HEART J. **15**:107 and 235, 1938.
6. Keith, N. M., and Osterberg, A. E.: The Human Tolerance for Potassium, Proc. Staff Meet. Mayo Clin., Oct. 2, 1946, p. 385.
7. Finch, E. A., Sawyer, C. G., and Flynn, J. M.: Clinical Syndrome of Potassium Intoxication, Am. J. Med. **1**:337, 1946.
8. Thomson, W. A. R.: Potassium and the T Wave of the Electrocardiogram, Lancet **1**:808, 1939.
9. Sharpey-Shafer, E. P.: Potassium Effects on T Wave Inversion in Myocardial Infarction and Preponderance of a Ventricle, Brit. Heart J. **5**:80, 1943.
10. Goldberger, Emanuel: Unipolar Lead Electrocardiography, Philadelphia, 1947, Lea & Febiger.
11. Goldberger, Emanuel: The Effect of Clockwise Rotation of the Heart on the Electrocardiogram, Am. J. Med. In press.

AURICULAR PAROXYSMAL TACHYCARDIA IN ASSOCIATION WITH MYOCARDIAL INFARCTION

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SUPRAVENTRICULAR tachycardia is extremely rare in association with myocardial infarction. Its frequency is suggested by its numerical relationship to auricular fibrillation, auricular flutter, and ventricular paroxysmal tachycardia. In the records of 1,247 patients in whom definite proof of myocardial infarction was found at the Los Angeles County Hospital, auricular fibrillation was observed in eighty-four patients,[1] auricular flutter in twenty,[2] ventricular paroxysmal tachycardia in fourteen, and supraventricular tachycardia in only five. Rosenbaum and Levine[3] in a study of 208 patients believed to have had their first attack of myocardial infarction found no instances of auricular paroxysmal tachycardia. Mintz and Katz[4] mention three instances in a group of 572 patients. Master, Dack, and Jaffe[5] verified supraventricular paroxysmal tachycardia by electrocardiograms in five of 300 patients who had myocardial infarction. This report is based upon the records of five patients observed in the Los Angeles County Hospital who were considered to have supraventricular tachycardia.

CASE REPORTS

CASE 1.—P. F. (No. 743-128), a Negro man 56 years of age, was admitted to the Los Angeles County Hospital on Oct. 7, 1941, because of a recent myocardial infarction. In electrocardiograms taken Oct. 8 and Nov. 26, 1941, there were indications of the expected serial changes of an anterior myocardial infarction (Fig. 1). He was discharged on Dec. 11, 1941.

On Dec. 18, 1941, he was readmitted because of increasing dyspnea, a swollen abdomen, and swelling of the ankles. There was a systolic murmur which was estimated as being of Grade 4 intensity. The liver extended 5.0 cm. below the right costal margin. The lower extremities were edematous to the mid-thighs. Digitalis was given, grains 3 of the powdered leaf three times daily for three days, and then grains 1½ daily. The electrocardiogram on December 19 showed no new changes in the pattern. He was discharged on Jan. 1, 1942, and was continued on digitalis, grains 1½ daily.

He was readmitted on Feb. 9, 1942. He had had almost constant pain in the upper right chest since his latest discharge and had had hemoptysis on two or three occasions. On the morning of Feb. 9, 1942, he suffered severe crushing, vise-like pains over the upper sternum. He was admitted at this time in shock; the blood pressure was 110/90 and the pulse was rapid and irregular with a rate of approximately 160 per minute. An electrocardiogram taken on February 9 revealed supraventricular tachycardia with changes consistent with another infarction. Evidence of

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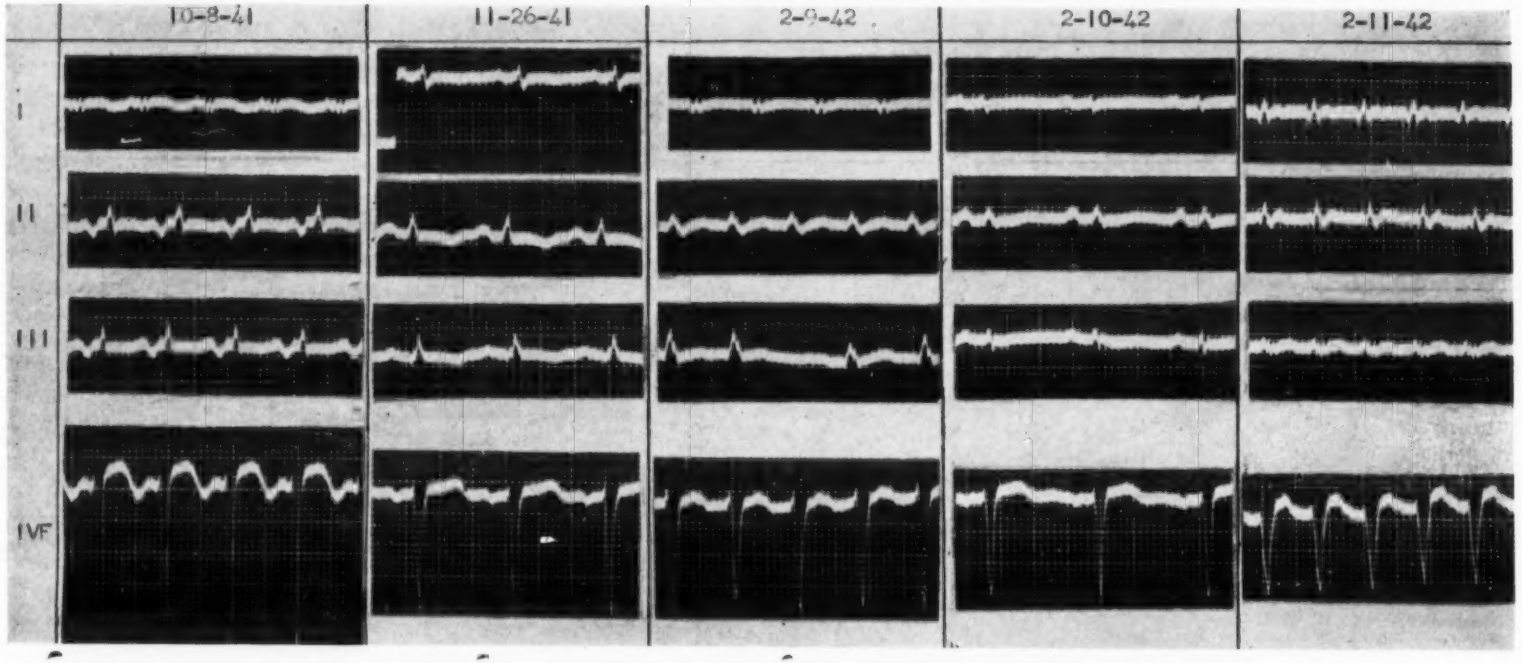

Fig. 1.—Case 1. Oct. 8, 1941, and Nov. 26, 1941: Anterior myocardial infarction.

Feb. 9, 1942: Supraventricular tachycardia. Auriculoventricular block, Lead III.
Feb. 10, 1942: Sinus rhythm.
Feb. 11, 1942: Supraventricular tachycardia.

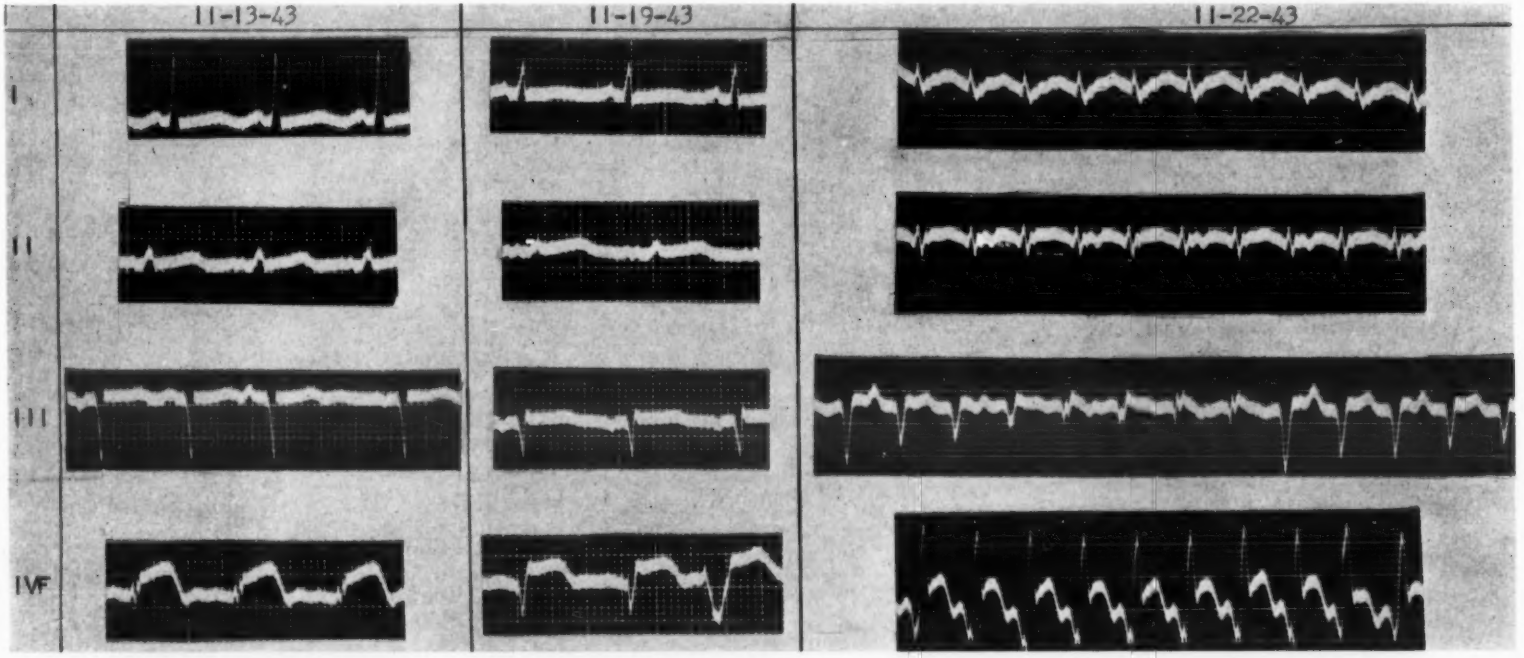

Fig. 2.—Case 2. Nov. 13, 1943: Anterior myocardial infarction. Auricular premature beat, Lead III.

Nov. 19, 1943: Anterior myocardial infarction. Ventricular premature beat, Lead IVF.
Nov. 22, 1943: Supraventricular tachycardia.

atrioventricular block was observed at several points in the tracing. No digitalis was given on February 9. On February 10, the electrocardiogram showed sinus rhythm. Digitalis, grains 3, was given on February 10 because of "increasing basal râles." The next morning, February 11, the tachycardia returned and the electrocardiogram revealed the existence of auricular paroxysmal tachycardia. The patient died suddenly at 1:10 P.M. No necropsy was obtained.

Comment.—It is difficult to analyze this case other than to comment that a ventricular rate of 160 imposed upon a very bad heart was an intolerable load.

CASE 2.—P. F. (No. 34-732), a woman 76 years of age, was admitted on Nov. 11, 1943. She had a history of diabetes and hypertension since 1923. Electrocardiograms made on November 13 and November 19 revealed a pattern of anterior myocardial infarction (Fig. 2). Auricular premature beats were seen in the tracing of November 13 and two ventricular premature beats in the tracing of November 19. On November 21, the patient developed sudden right hemiplegia and a regular tachycardia of 180 per minute. After the tachycardia appeared, digitalis was given in doses of 3 grains every four hours for six doses and then grains 1½ twice daily. Following the sixth dose (total dose of 18 grains), on November 22, the electrocardiogram revealed supraventricular paroxysmal tachycardia. The tachycardia continued and digitalis was continued, grains 1½ daily. The patient died suddenly on Nov. 26, 1943. No necropsy was obtained.

Comment.—Supraventricular paroxysmal tachycardia developed coincident with hemiplegia probably due to cerebral embolism from an intracardiac thrombus. The load which the persistent tachycardia which lasted five days imposed upon a badly damaged heart was intolerable.

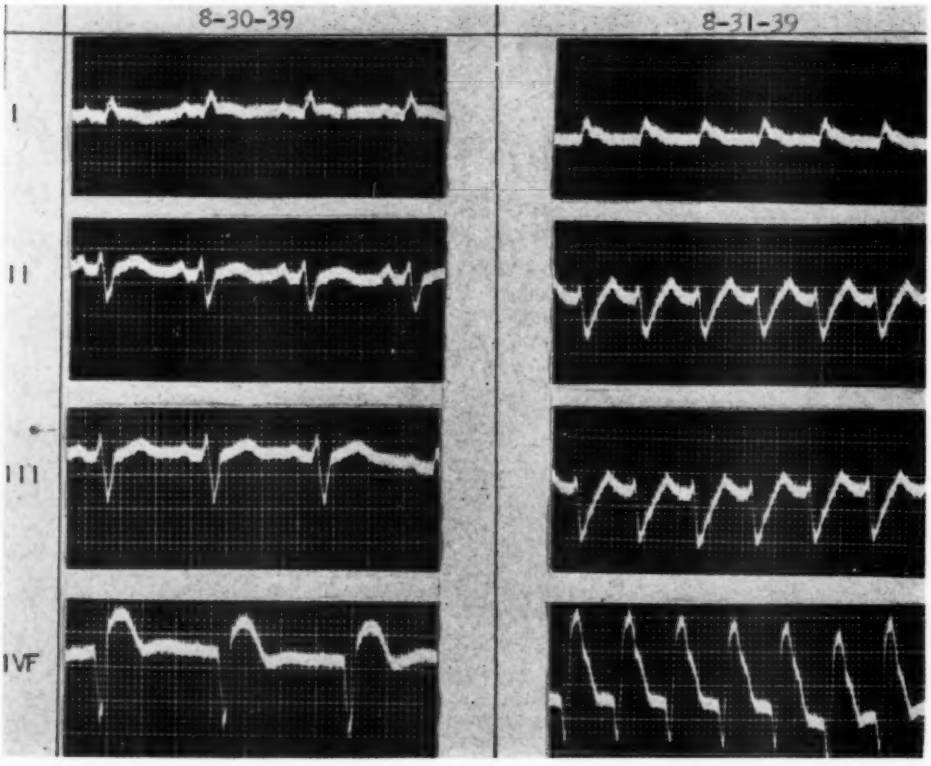

Fig. 3.—Case. 3. Aug. 30, 1939: Anterior myocardial infarction. Intraventricular conduction defect.
Aug. 31, 1939: Atrial paroxysmal tachycardia. Intraventricular conduction defect.

CASE 3.—P. F. (No. 609-955), a man 67 years of age, was admitted on Aug. 28, 1939. One week before, he had had knife-like, suffocating chest pain over the precordium radiating into the left side of the neck. He was dyspneic and apprehensive. A cold, clammy perspiration and a rapid, feeble pulse were present. The attack subsided in a few hours, but pain occurred daily and became continuous after the third day. On admission, because of pulmonary edema and distended cervical veins, he was given the powdered leaf of digitalis, grains 4½ every four hours for seven doses, and then grains 1½ daily. The patient received 33 grains in thirty-one hours. The next day he developed nausea and persistent vomiting. This was ascribed to overdigitalization. An electrocardiogram made on August 30 revealed a pattern of intraventricular conduction defect and anterior myocardial infarction (Fig. 3). On August 31, atrial paroxysmal tachycardia and intraventricular conduction defect were shown. Quinidine was then given in doses of 5 grains every four hours. The pulmonary edema increased, the tachycardia persisted, and the patient died at 12:50 A.M. on Aug. 31, 1939. No necropsy was obtained.

CASE 4.—P. F. (No. 608-060), a man 72 years of age, was admitted on May 8, 1938. Four days earlier he had developed sudden acute dyspnea and ankle swelling. Serial electrocardiograms made on May 9 and May 11 were considered consistent with anterior myocardial infarction (Fig. 4). He was discharged against advice on May 29, 1938.

He was readmitted on June 29, 1940. In the interim he had been dyspneic, needing two pillows in order to sleep, and for the past year, had had ankle edema. On the morning of June 29, he had had sudden substernal pain. He became orthopneic, cyanotic, and developed diffuse lung râles, left hydrothorax, and ankle edema. The liver, enlarged to the umbilicus, was tender and smooth. An electrocardiogram taken on July 1 showed the pattern of posterior myocardial infarction and intraventricular conduction defect with nodal rhythm. Digitalis was started on July 29 and a total of 24 grains was given. An electrocardiogram taken on July 2 showed supraventricular tachycardia. He died at 9:55 P.M. on July 2, 1940. A post-mortem examination revealed a recent posterior myocardial infarction and scars consistent with an old anterior lesion. The right coronary artery was occluded with a thrombus.

Comment.—Auriculoventricular nodal paroxysmal tachycardia developed following administration of 24 grains of digitalis in a man, 74 years of age, who had had a severe infarct two years after the initial attacks. He was digitalized because of right and left heart failure.

The patient and also the patient in Case 3 had bundle branch block, and the tachycardia in both patients, if seen without the previous tracings, could have been thought to be ventricular paroxysmal tachycardia. In both instances, large doses of digitalis were given and supraventricular tachycardia occurred the following day.

Auricular Paroxysmal Tachycardia in Association With Auricular Fibrillation.—The association of these two arrhythmias in heart disease other than acute myocardial infarction has been pointed out recently by Decherd and Herrmann[6,7] as not a rare occurrence. Auricular paroxysmal tachycardia is a rare complication of myocardial infarction, however, and its association with auricular fibrillation in this condition is extremely uncommon.

CASE 5.—P. F. (No. 541-863), a man 66 years of age, with no known previous cardiovascular disease, was admitted on April 22, 1940. An electrocardiogram taken on April 23 revealed the pattern of anterior myocardial infarction with auricular fibrillation and intraventricular block (Fig. 5). Digitalis was given in the following dosage: grains 28 of the powdered leaf in the first twenty-four hours and then grains 1½ daily. The next day, April 24, the electrocardiogram in the beginning of the tracing showed sinus tachycardia followed by a short run of auricular fibrillation, and the remainder represented auricular paroxysmal tachycardia. Quinidine was ordered in dosage of grains 3 four times daily. Despite the intraventricular block, the risk of the tachycardia seemed worse than that of the quinidine. The next day, April 25, sinus rhythm had returned. Digitalis, grains 1½ daily, was continued and quinidine, grains 3, was given after meals.

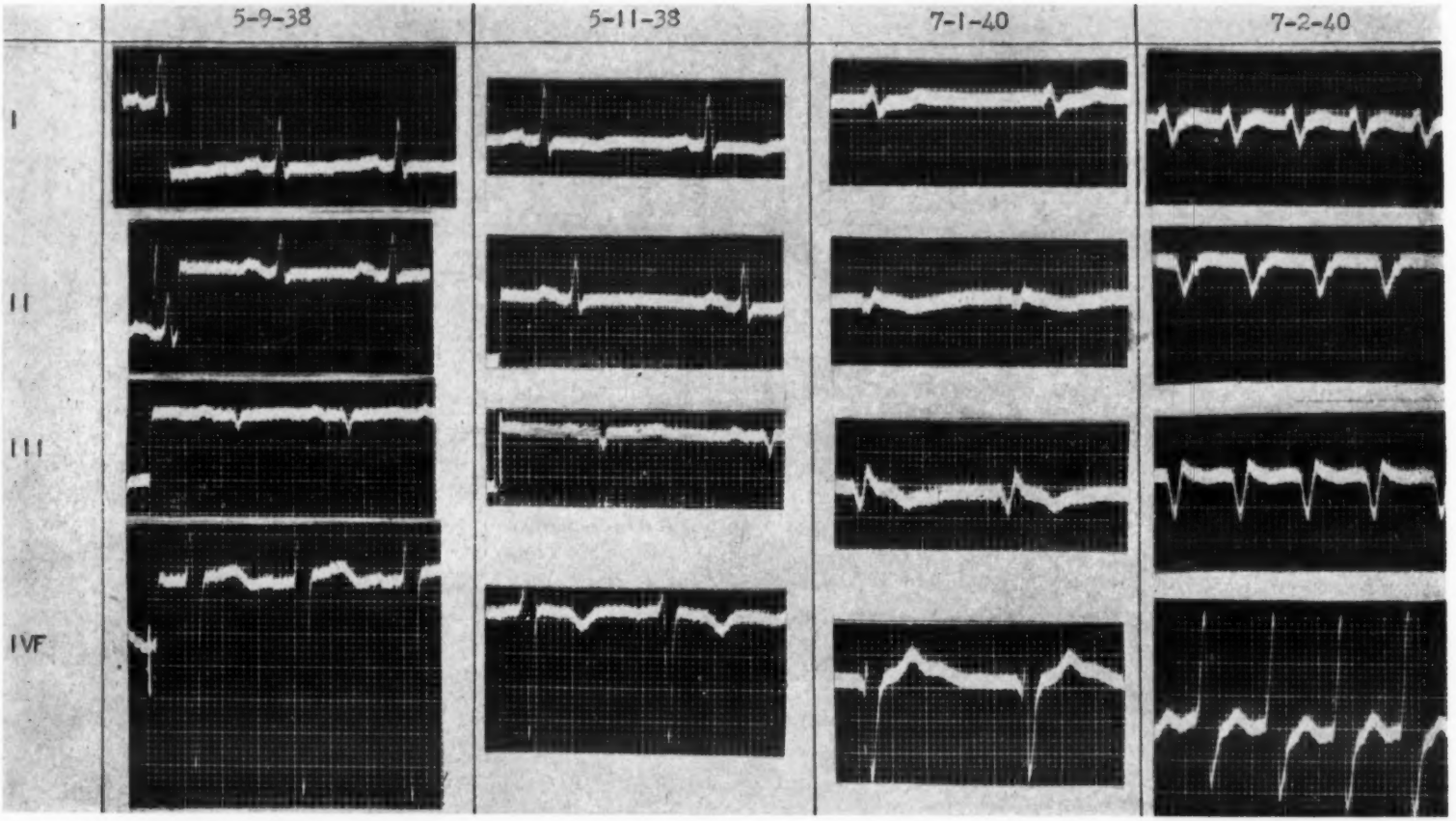

Fig. 4.—Case 4. May 9, 1938, and May 11, 1938: Anterior myocardial infarction.

July 1, 1940: Posterior myocardial infarction. Intraventricular conduction defect. Auriculoventricular nodal rhythm.
July 2, 1940: Supraventricular tachycardia. Auriculoventricular nodal origin. Rate 144.

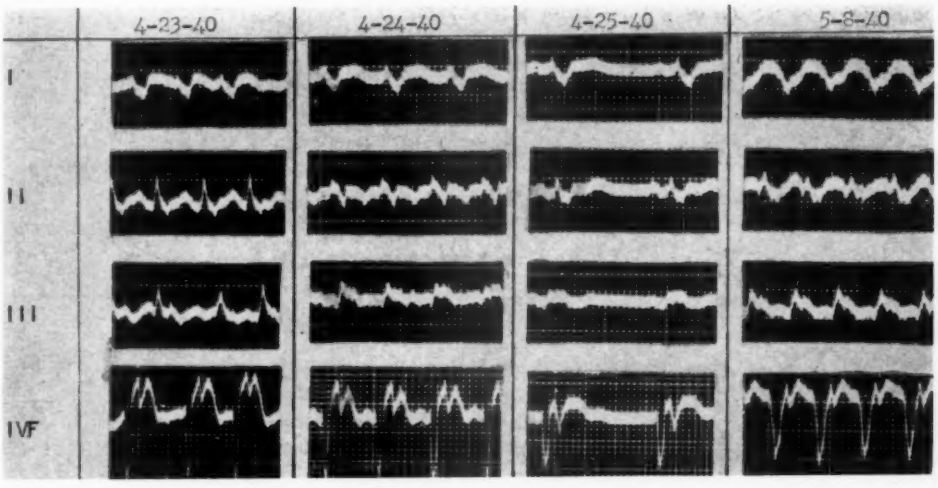

Fig 5.—Case 5. April 23, 1940: Auricular fibrillation. Intraventricular conduction defect. Anterior myocardial infarction.

April 24, 1940: Auricular paroxysmal tachycardia. Lead III isoelectric segment.
April 25, 1940: Sinus rhythm. Intraventricular conduction defect.
May 8, 1940: Auricular paroxysmal tachycardia. Lead III isoelectric segment.

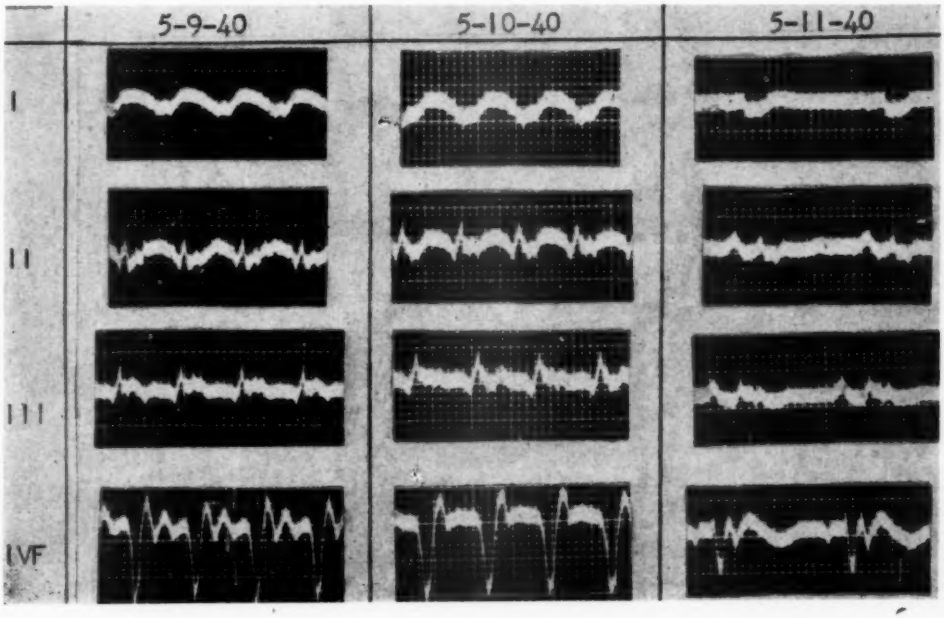

Fig. 6.—Case 5. May 9, 1940: Auricular paroxysmal tachycardia. Intraventricular conduction defect. Lead III isoelectric.

May 10, 1940: Auricular paroxysmal tachycardia.
May 11, 1940: Sinus rhythm. Intraventricular conduction defect.

On May 8 the arrhythmia was first diagnosed as auricular flutter with a ventricular rate of 190. A review of the tracing, however, indicates the arrhythmia to be auricular paroxysmal tachycardia at a little slower rate. Aside from the ventricular rate, which is rare for auricular flutter, there is a definite isoelectric segment present in Lead III. This has been emphasized by Decherd and Herrmann as the one dependable criterion for the differentiation of the two tachycardias in questionable cases. The patient's condition was so desperate, because of the continued tachycardia, that it was decided to give quinidine by vein. On May 9, 22 grains of quinidine dissolved in 400 c.c. of isotonic saline solution were administered. The tachycardia persisted and the electrocardiogram showed auricular paroxysmal tachycardia on May 10 (Fig. 6). The next day, May 11, the rhythm was normal but the patient had diffuse pulmonary edema, then developed pneumonia, and died two days later, May 13, 1940. Apparently heroic therapy in this case was useless, and death was ascribable to an uncontrolled ventricular rate of 200 per minute for four days.

Comment.—Although transitions from auricular fibrillation to auricular flutter are not uncommon in heart disease, transitions from auricular paroxysmal tachycardia to flutter or fibrillation are relatively uncommon. It apparently is a grave prognostic omen. Eight of the fourteen patients reported by Decherd and Herrmann died soon after they were observed. In only one was the diagnosis of myocardial infarction established.

DISCUSSION

Supraventricular paroxysmal tachycardia obviously is not an arrhythmia that is attributable to serious arteriosclerotic heart disease since it is found so rarely in myocardial infarction. It is true, however, that it occurred in the patients of our series with marked, long-standing heart damage. Probably all of these patients had had previous infarcts, and coronary atherosclerosis and ischemia were extreme. It is interesting and possibly significant that Rosenbaum and Levine found no instances of auricular paroxysmal tachycardia in their group of patients who presumably were suffering from their first attack. Master, Jaffe, and Dack[8] said that heart failure was present in all of their cases. It is apparent, therefore, that supraventricular tachycardia in relation to myocardial infarction is an arrhythmia which appears usually in those patients with extensive, long-existent heart damage.

Its appearance becomes of serious prognostic significance. Sinus tachycardia, which involves a ventricular rate only slightly over 100, is known to increase the mortality.[9,10] In a recent study of 572 patients at the Michael Reese Hospital, the mortality of the entire group was found to be 21.8 per cent. In the group with congestive failure, the mortality was 41.9 per cent. Mintz and Katz observed that "the combination of tachycardia and congestive failure is of graver prognostic significance than either alone." The greater load of a faster ventricular rate such as is produced by supraventricular tachycardia obviously should increase the mortality even more than sinus tachycardia, and it apparently does.

The gravity of supraventricular tachycardia should depend largely upon the degree of pre-existing damage and upon the duration of the tachycardia. Master and his co-workers found nine instances of paroxysmal tachycardia occurring in 300 patients with coronary artery thrombosis. All nine patients had heart failure and had an enlarged heart and hypertension. Of these, five were identified as supraventricular in origin by electrocardiographic tracings. One was

ventricular in origin. The other three patients had no tracings taken. Only two of the nine patients died. The tachycardia occurred in a group which enjoyed one of the lowest reported mortality rates (8 per cent). Furthermore, the duration of the tachycardia was less than twenty-four hours. The immediate mortality of the group of patients with myocardial infarction in which our five instances occurred was 51 per cent. In none of our patients did the tachycardia disappear. Three died within twenty-four hours after the onset of the tachycardia and two after its persistence for four and five days.

The question of the etiology of the arrhythmia is interesting. Decherd and Herrmann believe that digitalis in excessive amounts may precipitate auricular paroxysmal tachycardia. In three of our five patients, the arrhythmia followed the administration of large amounts of the drug within a short time. In Case 3 the patient received 33 grains within thirty-one hours and was obviously overdigitalized, as evidenced by persistent vomiting. In Case 4, 24 grains were given in twenty-four hours prior to the development of the arrhythmia. In Case 5, the patient received 28 grains the day preceding the onset of the arrhythmia. That the tachycardia in three of the five patients should follow large doses of digitalis would appear to be more than coincidence. This would tend to favor the belief of Decherd and Herrmann. They studied forty patients with auricular paroxysmal tachycardia and auriculoventricular block and found that twenty-three of these had received an obvious overdosage of digitalis.

In two of our patients digitalis was administered because of marked right and left ventricular failure. In the others, the presence of auricular fibrillation was the indication. Whether or not digitalis was the precipitating factor can only be conjectured. It does suggest the wisdom of not digitalizing too rapidly patients with myocardial infarction.

SUMMARY

Supraventricular tachycardia appeared in five instances only in 1,247 patients with myocardial infarction observed at the Los Angeles County Hospital. The mortality was 100 per cent.

It is a rare arrhythmia to be associated with myocardial infarction. It was usually associated with grave, long-standing heart damage. Its seriousness depends upon the degree of heart damage and the persistence of the tachycardia. It apparently followed overdigitalization in some instances. Prognostically, the appearance of supraventricular tachycardia in myocardial infarction would seem to be of grave portent.

REFERENCES

1. Askey, J. M., and Neurath, O.: The Prognostic Significance of Auricular Fibrillation in Association With Myocardial Infarction, Am. HEART J. 29:575-580, 1945.
2. Askey, J. M.: Auricular Flutter in Association With Myocardial Infarction; Its Prognosis and Management, Am. J. Med. (In press.)
3. Rosenbaum, F. F., and Levine, S. A.: Prognostic Value of Various Clinical and Electrocardiographic Features of Acute Myocardial Infarction; Immediate Prognosis, Arch. Int. Med. 68:913, 1941.
4. Mintz, S. S., and Katz, L. N.: Recent Myocardial Infarction; an Analysis of 572 Cases, Arch. Int. Med. 80:205, 1947.

5. Master, A. M., Dack, S., and Jaffe, H. L.: Disturbances of Rate and Rhythm in Acute Coronary Artery Thrombosis, Ann. Int. Med. **11**:735, 1937.
6. Decherd, G. M., and Herrmann, G. R.: The Association of Paroxysmal Atrial Tachycardia With Atrial Flutter or Fibrillation, AM. HEART J. **28**:457, 1944.
7. Decherd, G. M., and Herrmann, G. R.: Paroxysmal Supraventricular Tachycardia With A-V Block, AM. HEART J. **26**:446, 1943.
8. Master, A. M., Jaffe, H. L., and Dack, S.: The Treatment and the Immediate Prognosis of Coronary Artery Thrombosis (267 Attacks), AM. HEART J. **12**:549, 1936.
9. Levine, S. A., and Brown, C. L.: Coronary Thrombosis; Its Various Clinical Features, Medicine **8**:245, 1929.
10. Master, A. M., Dack, S., and Jaffe, H. L.: Coronary Thrombosis; an Investigation of Heart Failure and Other Factors in Its Cause and Prognosis, AM. HEART J. **13**:330, 1937.

Clinical Reports

SCOLIOSIS AND CARDIAC FAILURE

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CARDIAC or pulmonocardiac failure which results from severe deformity of the chest is not rare. The following case is reported because it illustrates many of the common clinical and pathological features of this condition.

CASE REPORT

A 19-year-old unmarried white girl, a patient of Dr. J. W. Martin, entered the hospital with the complaint of shortness of breath for three weeks. In 1929, at the age of 2½ years, the patient had acute anterior poliomyelitis. When first seen at the University Hospitals, at the age of 4, she was of normal size and fairly well nourished. There was weakness or paralysis of numerous muscles of the extremities and trunk. Without support, she was unable to sit up or to walk. Thoracic breathing was somewhat weaker than normal, but the respiratory excursion was equal bilaterally. The heart and lungs were normal. Bed rest, physiotherapy, and nightly splinting of the legs and feet resulted in no improvement at the end of one year. Numerous surgical procedures performed on the extremities during the years 1933 to 1938 resulted in the patient's being able to use crutches and to walk fairly well. She did not tolerate operations well, however, usually developing acidosis, slight fever, and tachycardia for several days postoperatively.

A left dorsal-right lumbar scoliosis was first noted in 1932. It progressed in severity until 1941. Celluloid jackets worn since 1933 had become impracticable by 1938 because of marked deformity of spine and chest. On examination in that year, the patient was poorly developed and considerably underweight, but no abnormalities of the heart or lungs were detected.

Beginning in 1943, the patient suffered frequent colds and easy fatigue and developed tachycardia and progressive dyspnea and orthopnea. In February, 1946, fourteen years after the onset of scoliosis and three weeks before death, her shortness of breath and palpitation increased greatly in severity and she had frequent epistaxis. Four days before her final admission to the hospital, her physician noted cyanosis, râles at the bases of the lungs, and accentuation of the second pulmonic sound. He began digitalization. On admission to the hospital she was deeply cyanotic, dyspneic, and orthopneic. The temperature was 38°C., the pulse rate 150, the respiratory rate 40, and the blood pressure 115/75. Basal râles and an apical systolic murmur were heard. There was minimal pitting edema of the ankles. She was placed in an oxygen tent and 20,000 units of penicillin, ¾ grain of sodium phenobarbital, and ⅛ grain of morphine were administered. Her condition rapidly grew worse and she died one hour and forty-five minutes after admission.

Autopsy (No. 9510).—The body was that of a poorly developed, moderately well-nourished young woman of immature appearance. The body weight was 28 kg. (61.6 pounds), the length 120 cm. (4 feet). Lips and nail beds were cyanotic and cervical veins were distended. The thorax

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was narrow and bulged forward on the right. On the left, rotation and angulation of the ribs displaced the medial margin of the scapula and produced a marked posterior protrusion. The trunk was greatly shortened, occupying only about one-fourth of the body length. The extremities showed varying degrees of muscular atrophy and the scars of numerous surgical operations.

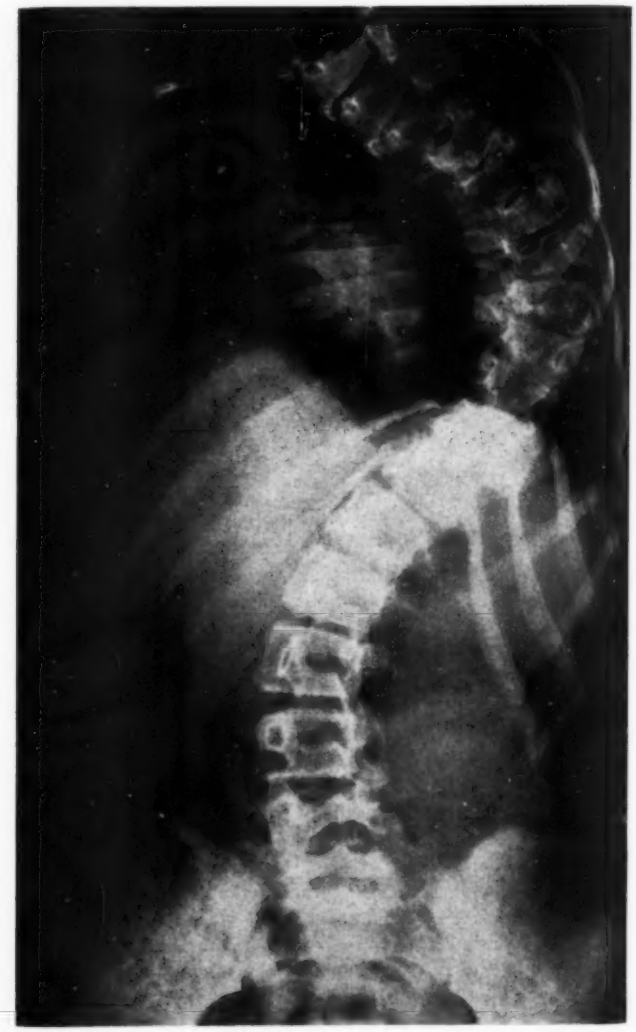

Fig. 1.—Roentgenogram of the spine, made at age of 8 years, four years after onset of scoliosis. The greatest degree of scoliosis is in the thoracic spine. Further progress of scoliosis occurred during the next five years.

All thoracic and lumbar vertebrae were involved in a U-shaped curve to the left, with its apex at the eighth and ninth thoracic vertebrae. The opposing surfaces of its arms were 16 cm. apart. The associated rotation of vertebrae to the left amounted to nearly 90° at the apex of the curve and the ribs were correspondingly deformed and displaced. The space between the apex of the spinal curve and the left ribs admitted only the tips of the fingers. A small portion of the left lung lay within this crevice. The remainder was anterior to the spine and partly overlaid it. The trachea was in the midline. The heart lay directly beneath the sternum and was rotated

about 10° to the left. The descending aorta followed the curve of the spine. The abdominal viscera occupied approximately normal positions.

The heart weighed 250 grams. The right atrium and ventricle were considerably dilated, the former to approximately twice the normal volume. The right ventricle was 6.0 mm. thick, the left ventricle 14 millimeters. Columnae carneae were enlarged and flattened, particularly in the right ventricle. Tricuspid, mitral, and aortic valves showed slight thickening and opacity without deformity. Coronary arteries, aorta, and pulmonary artery were normal.

The right lung weighed 370 grams, the left 350 grams. Both were small, the left particularly, and had the general appearance and texture of infantile rather than adult lungs. There was general moderate diminution of crepitancy, notably in the lower lobe of the left lung. Scattered foci of increased density up to 3.0 cm. in diameter were reddish purple, granular, and slightly elevated on section. Tissue elsewhere was dark red and moist. Alveoli were inconspicuous.

The liver weighed 820 grams. The central zones of its lobules were large and dark red. The spleen weighed 90 grams and had a wet, soft, purplish red cut surface. The kidneys weighed 100 grams each and showed prominence of small blood vessels. Other organs, including the brain, were grossly normal.

Microscopic Description of Lungs: The pleurae showed occasional small deposits of black pigment. In the parenchyma, particularly of the lower lobe of the left lung, there were many foci in which the lumina of alveoli were reduced and sometimes indistinguishable. Elsewhere, alveoli were sometimes distinctly dilated and their septa were shortened. In all sections, alveoli contained red blood cells, sometimes in large, dense foci, and numerous large mononuclear cells with faintly stained cytoplasm and vesicular oval nuclei containing finely granular chromatin. Occasional polymorphonuclear leucocytes were seen in alveoli, but they seldom formed appreciable aggregates. The bronchi contained similar cells. Blood vessels were dilated. Their walls were normal. Slight bronchiolar dilatation was an occasional observation.

Principal pathological diagnoses were cardiac hypertrophy and dilatation, especially manifest in right ventricle and atrium (cor pulmonale), moderate hypoplasia of the lungs, especially of the left lung, focal atelectasis of the lungs, focal chronic pulmonary emphysema, slight bronchopneumonia, atrophy of the anterior columns of the spinal cord consistent with healed poliomyelitis, scoliosis of the thoracic and lumbar vertebrae, and atrophy of skeletal muscle of the trunk and extremities.

COMMENT

The incidence of some degree of scoliosis following acute anterior poliomyelitis has been variously reported at 5 to 30 per cent.[1,2] According to Kleinberg,[1] in the majority of children scoliosis begins within five years after the acute illness and may progress throughout the remainder of the growth period. Maximum deformity has usually developed by the time the patient has reached young adulthood. The shortened life expectancy of persons in whom severe thoracic deformities have developed early in life has been long recognized.[3] Exceptions occur,[4] of course, but in seventy-nine cases collected by Chapman, Dill, and Graybiel,[5] the average age at death was 30 years. These authors, whose paper forms the basis for part of the following discussion, believe that pulmonocardiac failure is of common occurrence in severely deformed patients and is the most frequent cause of death.

The earliest and outstanding cardiorespiratory symptoms in severe deformity of the chest are dyspnea and tachycardia. These symptoms may persist for years, progressing slowly. Cough and epistaxis are frequent. Susceptibility to respiratory infections is increased and the effects of such infections are usually pronounced. A distinct intolerance to morphine has been frequently noted, administration of the drug having been followed by fatal respiratory depression

in numerous instances. The onset of severe dyspnea on slight exertion or attacks of paroxysmal dyspnea, asthma, great weakness, or fainting mark the beginning of pulmonocardiac failure. Death usually follows soon.

On physical examination the patients are small, frail, and dyspneic. Tachycardia is always present and the second pulmonic sound is frequently accentuated. Clubbing of the fingers does not occur. Cyanosis and edema are late signs, and the latter may never appear.

At autopsy, the lungs are small and are often described as resembling the lungs of children. Their small size has sometimes been attributed to hypoplasia; sometimes, with less reason, to atrophy. Focal pulmonary emphysema and atelectasis are often present and pneumonia of varying extent is found in the majority of cases. The most common cardiac abnormalities are hypertrophy and dilatation almost confined to the right ventricle. A shift in the position of heart or great vessels is an inconstant observation, seldom striking, and of doubtful significance. Edema and passive hyperemia of the viscera are frequent, but not often of great degree.

How deformity of the chest results in pulmonocardiac failure is not fully understood, but there is much to indicate that reduction of thoracic volume and faulty respiratory mechanics are chiefly responsible. The size of the lungs is limited by the small thoracic volume, and their effective size is further reduced by atelectasis and emphysema. To this static handicap is added the limitation of respiratory movement resulting from skeletal deformity and from weakness and poor mechanical effectiveness of the muscles of respiration.

Deficiencies in thoracic volume and respiratory excursion may have numerous secondary effects. The smaller size of the lungs reduces absolutely both the amount of air and blood which they can contain and the area of the interface where exchange of gases between air and blood can occur. Diminished respiratory excursion limits the normal inspiratory increase in the capacity of the lungs for air and blood and the normal increase in area of the interface. The increased breathing effort exerted in overcoming mechanical handicaps and maintaining gaseous exchange accounts for the characteristic dyspnea of severely scoliotic patients.

As has been indicated, two factors tend to reduce vascular capacity: (1) absolute reduction in number and size of vessels and (2) curtailment by diminished pulmonary expansion of the expansion of blood vessels which normally occurs in inspiration.[6,7] Since cardiac output is not reduced in the majority of scoliotic patients in whom it has been studied,[5] the effect of reduced vascular capacity is to increase pulmonary arterial resistance.* There is evidence, also, that in certain chronic pulmonary disorders, including kyphoscoliosis, the associated increase in ventilatory effort is accompanied by a greater than normal inspiratory increase in right ventricular output; an increase dependent on increase in negative intra-

*Since this report was submitted for publication, attention has been drawn to the possibility that in kyphoscoliosis, oxygen lack resulting from poor ventilation of the lungs may induce local constriction of pulmonary arterioles and precapillaries with resultant increase in pulmonary arterial resistance. (McMicheal, J.: Heart Failure of Pulmonary Origin, Edinburgh M. J. **55**:65, 1948.)

The existence of pulmonary arterial hypertension in kyphoscoliosis has been demonstrated. (Medical Grand Rounds, American Practitioner **2**:764, 1948.)

thoracic pressure.[8,9,10] To the extent that the expansibility of the lungs may be reduced in these disorders, as by pulmonary fibrosis, it is likely that change in intrathoracic pressure is not accompanied by a normal proportionate change in pulmonary volume. It may be, therefore, that during each inspiration the discrepancy between right ventricular output and pulmonary vascular capacity is widened. Moreover, a pumping action on the lesser circulation, which Macklin[11] believes is exerted by stromal pull on pulmonary vessels during inspiration and by elastic recoil of the lungs during expiration, would presumably be reduced as a result of diminished respiratory excursion in thoracic deformity. If the view is correct that the action of this "pulmonary accessory heart" is normally beneficial,[7] it can be argued that a reduction of such pumping action is deleterious to cardiocirculatory function. It is recognized, however, that the concept of a pulmonary accessory heart, though plausible, is unproved.

Once pulmonocardiac failure begins, available therapeutic measures offer little hope of recovery. Rest, digitalis, and diuretics are largely ineffective, and morphine is often contraindicated. The goal of medical care in deformed patients is therefore the prevention of pulmonocardiac failure. In its attainment, general hygienic measures and the avoidance of respiratory infections are the principal considerations.[5]

Prevention of deformity itself is, of course, the primary objective. Such prevention requires first the recognition of the likelihood of scoliosis following acute anterior poliomyelitis and of the likelihood of its progression to severe deformity. Second, it requires that measures undertaken after the acute illness be directed no less intensively at preventing scoliosis than at preventing other musculoskeletal defects. The well-known difficulty of correcting or even halting the progression of paralytic scoliosis emphasizes this point. Finally, if scoliosis develops and progresses despite preventive measures, efforts at correction of the deformity, probably including spinal fusion, support, and muscle training, must be well planned, prompt, and unremitting.

SUMMARY

A typical case of cardiac failure in a patient with paralytic scoliosis is reported.

Important effects of thoracic deformity are to limit pulmonary ventilation, to impede the pulmonary circulation, and to alter respiratory fluctuations in blood flow. Increased ventilatory effort, tachycardia, and right ventricular dilatation and hypertrophy are thereby induced. If these responses can be considered compensatory, they are inadequate to permit normal development and activity and they ultimately fail completely.

Treatment is largely preventive, and begins with prevention or correction of the thoracic deformity itself.

REFERENCES

1. Kleinberg, S.: Paralytic Scoliosis: Analysis of 51 Cases, Am. J. Surg. **64**:301, 1944.
2. Colonna, P. C., and Vom Saal, F.: Study of Paralytic Scoliosis Based on 500 Cases of Poliomyelitis, J. Bone & Joint Surg. **23**:335, 1941.
3. Adams, Francis: The Genuine Works of Hippocrates, Baltimore, 1939, Williams & Wilkins Company, p. 323.
4. Kerwin, A. J.: Pulmonocardiac Failure as a Result of Spinal Deformity, Arch. Int. Med. **69**:560, 1942.
5. Chapman, E. M., Dill, D. B., and Graybiel, A.: The Decrease in Functional Capacity of the Lungs and Heart Resulting From Deformities of the Chest: Pulmonocardiac Failure, Medicine **18**:167, 1939.
6. Dupee, C., and Johnson, V.: Respiratory Changes in Pulmonary Vascular Capacity, Am. J. Physiol. **139**:95, 1943.
7. Macklin, C. C.: Length and Width Changes in Pulmonary Arterial System of Rabbits in Passing From Stage of Expiration to That of Collapse as Revealed by Roentgenography, Dis. of Chest **11**:590, 1945.
8. Bloomfield, R. H., Lauson, H. D., Cournand, A., Breed, E. S., and Richards, D. W., Jr.: Recording of Right Heart Pressure in Normal Patients and in Patients With Chronic Pulmonary Disease and Various Types of Cardiocirculatory Disease, J. Clin. Investigation **25**:639, 1946.
9. Lauson, H. D., Bloomfield, R. A., and Cournand, A.: The Influence of Respiration on the Circulation in Man, Am. J. Med. **1**:315, 1946.
10. Shuler, R. H., Ensor, C., Gunning, R. E., Moss, W. G., and Johnson, V.: The Differential Effect of Respiration on the Left and Right Ventricles, Am. J. Physiol. **137**:620, 1942.
11. Macklin, C. C.: Terminal Pulmonary Venules in Mammalian Lungs, Tr. Roy. Soc. Canada (Sect. V., Biol. Sc.) **39**:105. 1945.

CORONARY ARTERIOVENOUS FISTULA

Case Report

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THE following case report describes a congenital cardiovascular anomaly unique in our experience and, we believe, not hitherto suggested as a possible diagnosis during life. A similar anomaly, discovered incidentally at autopsy, has been the subject of a report by Halpert.[1]

R. P., a boy of 9 years, was admitted to the Surgical Service of the Massachusetts General Hospital on June 24, 1947, for study of a continuous murmur heard maximally in the right parasternal region. His mother stated that she had been in good health during her pregnancy and that the child was delivered uneventfully. (The record of the hospital where the child was delivered does not mention any cardiovascular abnormalities.) He developed normally during infancy but at the age of 2 years was admitted for a few days to another hospital because of a transient right hemiplegia of unknown cause. The hospital record of this illness stated that a loud apical systolic murmur was present. When 5 years old, the boy became ill with scarlet fever, and his family physician also noted the presence of a heart murmur and referred him to the Massachusetts General Hospital for evaluation of his cardiac status. There had been no joint pains or other symptoms suggestive of rheumatic fever.

When first seen in the Out Patient Department on May 15, 1943, the child was entirely symptom free and appeared to be in good health. The only abnormalities described were enlargement of the tonsils, questionable cardiac enlargement, and the presence of a loud apical systolic murmur followed by a third sound and a short diastolic rumble. An electrocardiogram was normal. Chest x-ray films were not remarkable except for slight cardiac enlargement (Fig. 1). Over the course of the next four months other examiners noted the disappearance of the diastolic rumble, and it was observed that the systolic murmur described as "apical" was actually loudest along the lower right sternal border and in that area was part of a definite continuous murmur.

During the subsequent three and one-half years the patient remained in good general health without any complaints suggestive of an impaired cardiac reserve, and with no change in the physical findings. He underwent a tonsillectomy in 1945 and a circumcision in 1946 without difficulty.

In view of the continuous character of the murmur, the diagnosis was made of an arteriovenous fistula, the exact location of which was in doubt (the chest wall, right lung, and internal mammary and coronary vessels were all mentioned as possibilities). If the patient had also had rheumatic fever with myocarditis following scarlet fever at the age of 5 years as an explanation for the transient apical diastolic rumble, there was no longer any clear evidence of rheumatic heart disease. Since it was believed possible that the continued existence of the arteriovenous fistula might result in significant myocardial strain over the course of time, and because it also appeared possible that this fistula might be excised, operation was advised.

On admission to the Surgical Service on June 24, 1947, he was seen to be a well-developed and well-nourished young boy, who was not dyspneic on effort and who showed no cyanosis.

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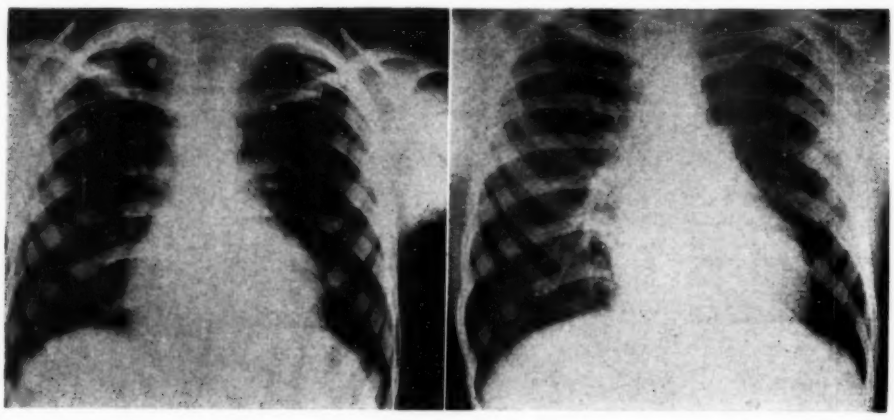

Fig. 1.—Chest x-ray films showing slight cardiac enlargement. *A*, May 18, 1943; *B*, May 8, 1947.

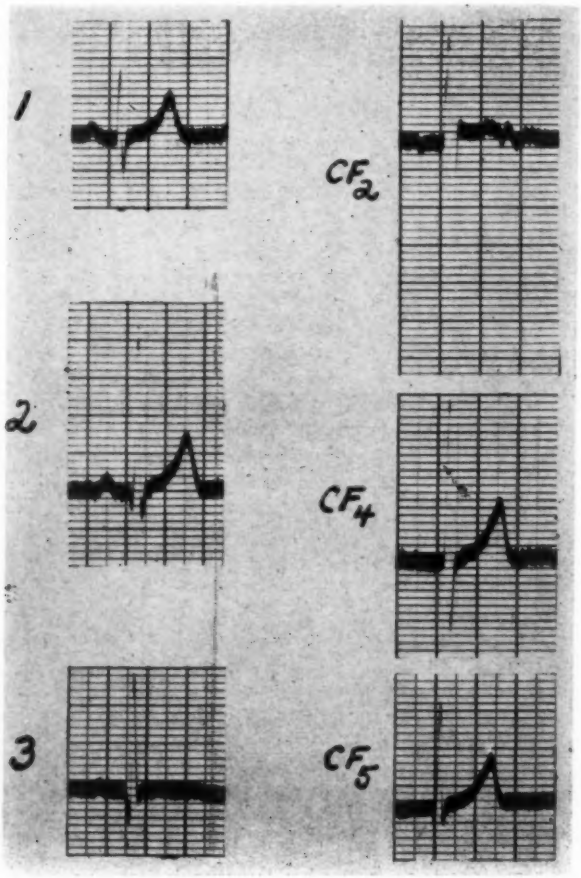

Fig. 2.—Electrocardiogram taken May 16, 1947, showing normal complexes throughout.

The pulse rate was 72 and the blood pressure was 110/75. The pupils reacted normally to light and accommodation, the throat was clean, and the carotid pulsations were equal bilaterally. The neck veins were not remarkable. The thoracic cage was normally proportioned, and the lung fields were resonant and clear. Examination of the heart showed the maximal apex impulse to be at the left midclavicular line in the fifth intercostal space. The second sound in the pulmonic area was louder than the second aortic sound. In the fourth right intercostal space adjacent to the sternal border there was heard a continuous murmur, the systolic component of which was of Grade 3 intensity. The systolic phase of this murmur was well heard at the cardiac apex and at the base of the heart but was not transmitted to the lung bases or down the spine. No thrill was present, and no other murmurs were heard. The liver and spleen were not palpable, there was no edema, and the peripheral pulsations were normal. There was no clubbing of the fingers or toes.

Routine blood studies were not remarkable, and a urine specimen was negative. The blood Hinton reaction was negative. Chest x-ray films taken one month previously (Fig. 1) were reviewed and were considered to show normal lung fields and a heart shadow which was at the upper limits of normal in size or possibly slightly enlarged. The shape of the heart was not characteristic of any specific pathological condition. An electrocardiogram (Fig. 2) was also within normal limits.

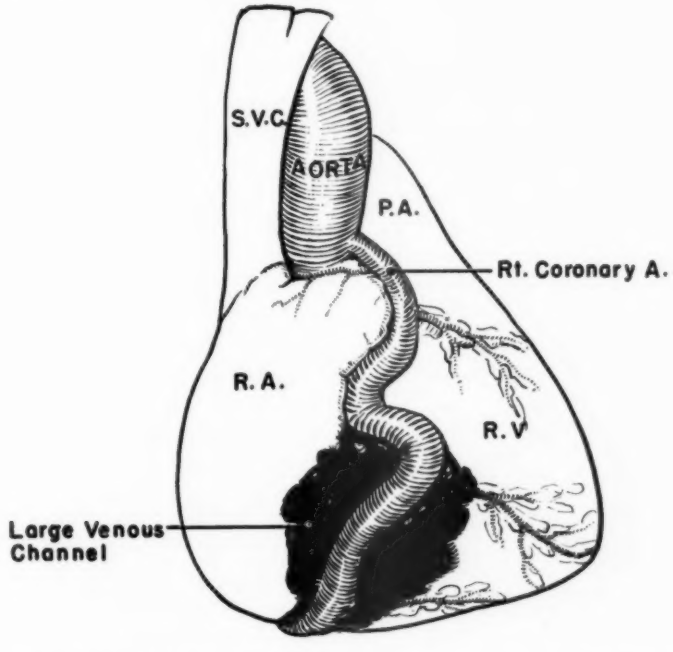

Fig. 3.—Drawing (based on a sketch made at operation) showing the relative size and position of the right coronary artery and the dilated venous channel.

On June 25, 1947, an exploratory thoracotomy was performed (by R. H. S.). The operative note reads as follows:

A long oblique incision was made across the right chest which was opened through the sixth intercostal space. This gave an excellent exposure. The lung was not adherent. It was found on palpation and inspection to be completely normal. Inspection of the anterior thoracic wall showed no evidence of a fistula in the internal mammary vessels, but it soon became apparent that there was an abnormal coronary artery which could be seen through the thin pericardial layer. The pericardium was then incised and retracted so as to give a good exposure of the

right portion of the heart. The right coronary artery was enormously dilated and tortuous (Fig. 3). At its origin from the ascending portion of the aorta it was felt to be about 6.0 mm. in diameter. In its widest portion as it descended along the auriculoventricular groove it was about 1.0 cm. in diameter and very thick walled. The vessel continued in its usual course around posteriorly where it appeared to meet with a large venous channel in the wall of the auricle. This was undoubtedly the coronary vein as it emptied into the coronary sinus. It seemed unlikely that anything could be accomplished surgically in this case by ligation of this vessel, excision, or otherwise, without serious damage to the circulation to the heart muscle and it seemed unlikely also that this defect was causing him any serious difficulty. It was therefore decided that nothing should be done. The incision in the pericardium was closed with fine silk sutures and the lung was expanded. The chest wall was then closed, using pericostal sutures of catgut, with silk in the remaining layers, the postoperative diagnosis being arteriovenous fistula between the right coronary artery and right coronary vein.

It was observed during the procedure that a marked thrill could be felt by placing the gloved finger over this group of abnormal vessels.

The patient recovered uneventfully from the operation and was discharged from the hospital on July 7, 1947. When last seen on Dec. 9, 1947, he was in excellent health, attending school, and leading a normal life. The physical findings were unchanged.

COMMENT

It would be unwise to try to predict too accurately the outcome in this case. Halpert's[1] patient, also male, died at the age of 54 years from carcinoma of the stomach without obvious symptoms of heart disease. (Indeed, no evidences of cardiovascular abnormality were detected during life.) At autopsy the heart was found to be hypertrophied, weighing 500 grams; a large, tortuous right coronary artery, 1.5 to 2.0 cm. in diameter, was present which emptied into the coronary sinus via an anastomotic loop. This loop also was markedly tortuous and on microscopic study its structure was seen to be intermediate between artery and vein. The similarity between the findings in this case and in ours is striking. We believe that the importance of the abnormal coronary arteriovenous communication in our patient probably lies not so much in its effect on the blood supply to the myocardium (doubtless an adequate collateral circulation from the left coronary artery is present) as in its useless diversion of a portion of the left ventricular output back into the right auricle, and in the fact that it is a potential locus for baterial endarteritis. However, since congenital arteriovenous fistulas of this caliber are as a rule remarkably well tolerated, we do not anticipate difficulty for many years.

We have encouraged this boy to lead a normal life, have advised semiannual examinations to evaluate his cardiac status, and have recommended the administration of penicillin prior to any dental extraction.

SUMMARY

A 9-year-old boy was operated upon to ascertain the origin of a continuous murmur heard maximally over the lower right sternal border. At operation an arteriovenous fistula connecting the right coronary artery and vein was discovered.

ADDENDUM

Dr. Robert E. Gross of the Children's Hospital, Boston, has kindly permitted us to include the following note on a patient on whom he has operated. A 16-year-old boy was admitted to the Children's Hospital in January, 1947, with a history of known heart disease since infancy. A diagnosis of patent ductus arteriosus complicated by streptococcal bacterial endarteritis had been made six weeks previously and the patient successfully treated with penicillin. On admission, a harsh continuous murmur associated with a thrill was present, maximal over the third and fourth intercostal spaces along the left sternal border. An exploratory operation was performed by Dr. Gross on Jan. 27, 1947, at which time an abnormal area characterized by bulging and thinning of the myocardium was found in the lateral wall of the left ventricle, located 2.0 to 3.0 cm. below and in front of the tip of the left auricle, about 3.5 cm. in diameter and associated with a thrill. The identity of any major vessels feeding into this region was not ascertained. No further surgery was undertaken, and the patient recovered uneventfully. The postoperative diagnosis. was arteriovenous aneurysm, probably of the coronary system.

REFERENCE

1. Halpert, B.: Arteriovenous Communication Between the Right Coronary Artery and the Coronary Sinus, Heart 15:129, 1930.

VAGOVAGAL SYNCOPE: REPORT OF A CASE APPARENTLY INDUCED BY DIGITALIZATION

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DESCRIPTIONS of vertiginous, syncopal, and convulsive attacks associated with a slow pulse have been described by Gerbezius (1719), Morgagni (1761), Adams (1826), Stokes (1846), and others. These attacks have become known as the Adams-Stokes syndrome, and a number of mechanisms for their production have been described. Many of these mechanisms are associated with low heart rates, all are associated with lowered or absent peripheral pulse, and all produce vertigo, syncope, or convulsions by reduction of blood flow through the brain.

Attempts at more exacting definition of the syndrome, by the inclusion of criteria not obtainable from history or clinical examination, have led to confusion in the use of the term. One commonly employed definition limits its use to seizures wherein atrioventricular block with prolonged ventricular diastole is present[1]; another, to heart block with ventricular standstill, tachycardia, fibrillation, or a combination of these.[2] Both definitions necessitate the use of infrequently available equipment at the time of the attack, inasmuch as the changes may be transient and present only at that time. Both eliminate those disturbances of cardiac rhythm, other than atrioventricular block, which may be associated with a slow or absent peripheral pulse. We fail to see the usefulness of such technical limitations (often impracticable of application because of the transient nature and unpredictable occurrence of the seizures) in a syndrome whose chief usefulness appears to be a simple, ever ready method of broadly differentiating the vertiginous, syncopal, or convulsive seizures of cardiac origin from those of metabolic, cerebral, or other origin. The definition first stated allows inclusion of the cases reported by Gerbezius, Adams, and Stokes, where the mechanism of the slow pulse was not graphically recorded and proved, those of Morgagni, where one case is somewhat suggestive of a reflex origin of the syndrome, as well as inclusion of the numerous cases reported where the Adams-Stokes episodes occurred before permanent heart block was present and failed to occur thereafter. To be retained in medical literature as a syndrome, the term must have a descriptive clinical significance and should include all the cardiac mechanisms producing a slow or imperceptible pulse with syncope.

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The mechanisms which might be included under this syndrome are: (1) paroxysmal auricular standstill with ventricular arrest; (2) paroxysmal and intermittent atrioventricular block with ventricular arrest; (3) permanent complete atrioventricular block associated with intermittent alteration of the sensitivity of the idioventricular pacemaker, with temporary alteration of the vascular tone, or with an increased metabolic demand not met by an increase in heart rate or stroke output; and (4) paroxysms of rapid ventricular beating (ventricular tachycardia, flutter, or fibrillation) with inaudible heart sounds and absent peripheral pulse.

The etiological factors described as responsible for producing these mechanisms include: (1) reflex mechanisms of carotid sinus-vagal, vagovagal, vasovagal, and central vagal types; (2) toxic or infectious lesions with reversible damage of the conduction system due to diphtheria, the rheumatic state, syphilis, trichiniasis, quinidine, digitalis, and strophanthus; (3) temporary anoxia of the conduction system seen in certain forms of rapid heart action, coronary sclerosis, myocardial infarction, and anoxia from obstructed airway, altitude, or oxygen-poor atmosphere; (4) permanent destruction of the conduction system about the auriculoventricular node from abscess, granuloma, neoplasm necrosis, or scarring; and (5) congenital defect of the conduction system.

In the neurogenic group, those of vagovagal origin apparently are infrequent, and especially infrequent are those of vagovagal origin in which the hyperactive reflex is associated with a diverticulum of the esophagus.

Weiss and Ferris[3] in 1934 described the first case of which we are aware of transient complete heart block in association with an esophageal diverticulum. Their patient was a 64-year-old white man without evidence of organic heart disease, who was studied after he was admitted to the hospital because of attempted suicide. For ten years he had suffered from intermittent fainting attacks induced by swallowing. Barium esophogram revealed an anterior "hooked" traction diverticulum at the junction of the middle and lower one-third of the esophagus, associated with dilatation of the lower one-third. Electrocardiographic studies were not obtained during the syncopal attacks, but the heart rate was found to be slow and irregular. These authors were able to reproduce the attacks by inflating a rubber balloon at the level of the diverticulum. Electrocardiograms recorded during balloon inflation revealed atrioventricular dissociation with a slow, irregular ventricular rhythm. Adrenalin and ephedrine prevented the syncope by means of the ready development of an idioventricular rhythm of approximately normal rate. Atropine abolished the syncope by preventing the atrioventricular block.

We have observed a patient who is an example of vagovagal syndrome secondary to an esophageal diverticulum. There was associated a vagal type of carotid sinus sensitivity. The patient is of interest because of the infrequency of reported cases of this type and because of observations concerning the mechanism of symptom production.

CASE REPORT

A 67-year-old white man presented himself on Dec. 10, 1941, at the Milwaukee County Hospital Out-Patient Clinic, complaining of choking, vomiting, fullness beneath the xiphoid process, dizziness, and fainting on eating or swallowing. These symptoms had been present for a single day. He had been receiving digitalis since April, 1941, because of breathlessness on exertion, which appeared to be due principally to chronic bronchitis and emphysema. Sipping water, precordial percussion, and pressure over the right carotid sinus produced asystole together with weakness, vertigo, syncope, and occasional epileptiform twitchings. Pallor and hypotension accompanied these episodes.

Electrocardiograms obtained at that time (Fig. 1,*A*) showed depression of the RS-T segment and flattening of the T wave suggestive of a digitalis effect. Tracings obtained under the test conditions named revealed the development of incomplete and complete atrioventricular block with a slow, irregular ventricular rhythm (Fig. 1,*B* and *C*). An esophogram revealed an "anterior diverticulum at the junction of the middle and distal one-third with dilatation of the distal one-third of the esophagus apparently due to obstruction at or near the cardia."

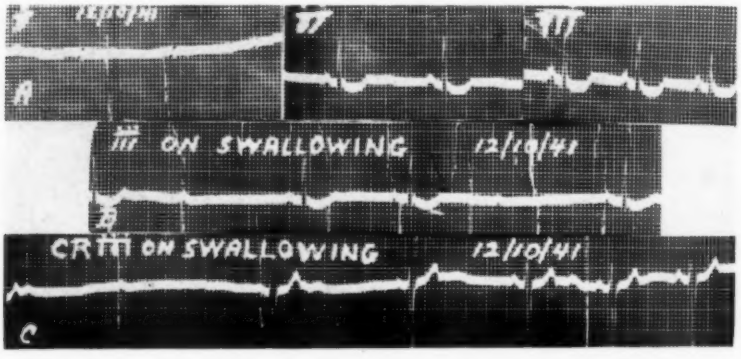

Fig. 1.—Electrocardiogram taken Dec. 10, 1941, at the time of spontaneous syncopal attacks produced by swallowing. Esophagram at this time revealed dilatation of the distal one-third due to obstruction at or near the cardia.

***A*, Leads I, II, and III. Note the downward convexity of the S-T segments and low amplitude of the T, compatible with digitalis effect.**

***B*, Lead III, on swallowing, showing the development of low-grade atrioventricular block.**

***C*, Lead CR_3, on swallowing, showing the development of low-grade atrioventricular block.**

The symptoms cleared after the patient was given atropine, although carotid sinus stimulation continued to produce vertigo with insufficient cardiac slowing to cause syncope. Since 1941, he has experienced only one brief recurrence of symptoms which were reported to have been rapidly relieved by atropine followed by esophageal dilatation. He has continued to take digitalis constantly throughout the five-year period.

CLINICAL OBSERVATIONS

In November, 1946, a series of observations was begun on this patient in order to study the mechanism of production of the Adams-Stokes attacks. These observations are summarized in the following.

Observations From the History.—The syncopal attacks which appeared during swallowing occurred only when there was esophageal dilatation, apparently secondary to cardiospasm.

These attacks were associated with sinus bradycardia and incomplete and complete atrioventricular block with slow and irregular ventricular rhythm. This accounted for the pallor and moderate-to-profound hypotension, and when the attacks were prolonged, they produced cerebral anoxia of sufficient degree to cause syncope and convulsive twitchings.

There was hypersensitivity of the right carotid sinus of sufficient degree to produce syncope only during episodes of esophageal dilatation.

Atropine relieved the attacks primarily through its interference with the vagal reflex and secondarily by its relief of the cardiospasm.

The patient was receiving full therapeutic doses of digitalis on both occasions when spontaneous attacks occurred.

Observations From Study of the Patient While on Full Therapeutic Doses of Digitalis Without X-ray Evidence of Esophageal Dilatation or Clinical Symptoms.—These studies were made with the use of a Miller-Abbott tube inserted in the

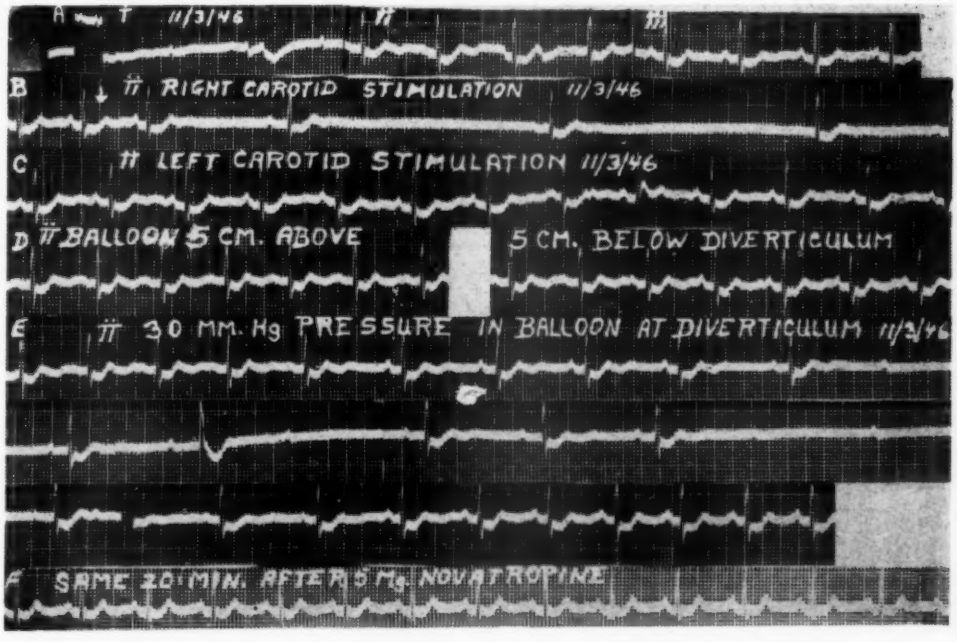

Fig. 2.—Electrocardiogram taken Nov. 3, 1946. Patient on digitalis. No evidence of esophageal dilatation or clinical symptoms. Tracings taken with Miller-Abbott tube in esophagus.

A, Leads I, II, and III after insertion of the tube.

B, Lead II during right carotid sinus stimulation. Sinus arrest with development of slow idioventricular rhythm is present.

C, Lead II during left carotid sinus stimulation. No change in the rate or rhythm is noted.

D, Lead II with the balloon in the esophagus 5.0 cm. above and below the level of the diverticulum and distended with air to a pressure of 80 mm. of mercury. No change in the rate or rhythm is noted in either tracing.

E, Continuous tracing of Lead II with the balloon at the level of the diverticulum distended with air to a pressure of 30 mm. of mercury. There is depression of the sinoauricular node, low-grade atrioventricular block, and occasional cycles of ventricular escape.

F, Lead II twenty minutes after subcutaneous administration of 5.0 mg. of novatropine with the balloon at the level of the diverticulum distended with air to a pressure of 120 millimeters of mercury. The rate and rhythm of the heart are unaltered.

esophagus and inflated by a bulb. The pressure in the balloon was measured by a mercury manometer attached to the Miller-Abbott tube by means of a rubber T tube. Electrocardiograms were routinely recorded, Lead II being used.

Right carotid sinus pressure (Fig. 2,*B*) produced sinus arrest with the development of a slow, irregular idioventricular rhythm. Pressure was released when vertigo became severe.

Left carotid sinus pressure produced no appreciable symptoms or electrocardiographic changes (Fig. 2,*C*).

When the balloon was inserted in the esophagus a distance of 5.0 cm. above or below the diverticulum and inflated with air to a pressure of 80 mm. Hg, there was no appreciable alteration of the heart rate or rhythm (Fig. 2,*D*). The patient's only complaint was uncomfortable substernal fullness or distress.

At the level of the diverticulum, distension of the balloon to a pressure of only 30 mm. Hg produced vertigo, pallor, depression of the sinoauricular node, and low-grade atrioventricular block with occasional cycles of ventricular escape (Fig. 2,*E*).

Atropine sulfate or novatropine, given subcutaneously or orally, effectively prevented the development of bradycardia or arrhythmia on inflation of the

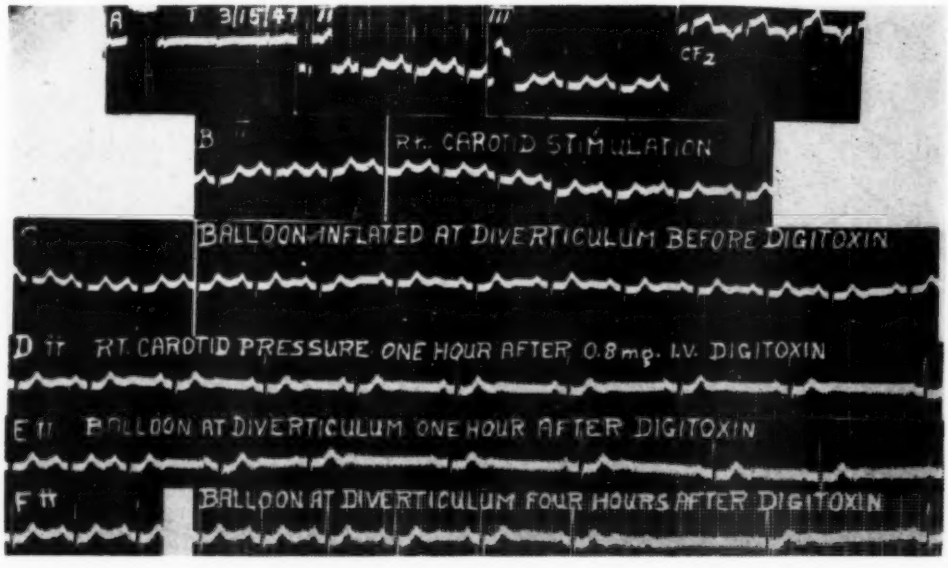

Fig. 3.—Electrocardiograms taken March 15, 1947, three weeks after digitalis was discontinued.

***A*, Leads I, II, III, and CF_2 with the balloon inserted in the esophagus but not distended with air.**

***B*, Lead II during right carotid sinus stimulation. Stimulation was applied at the time of the broad vertical line on the tracing. No change in rate or rhythm is noted.**

***C*, Lead II with the balloon at the level of the diverticulum and inflated with 100 c.c. of air. There is slowing of the heart rate from 100 to 60 beats per minute and minor alterations of the P, probably evidence of downward displacement of the seat of impulse formation in the node.**

***D*, Lead II showing the effect of right carotid sinus stimulation one hour after intravenous administration of 0.8 mg. of digitoxin. Note the increased cardiac slowing.**

***E*, Lead II taken immediately after *D*, with the balloon at the level of the diverticulum and inflated with 80 c.c. of air. Note the marked bradycardia and changes in the form of the P.**

***F*, Lead II taken four hours after the digitoxin, with the balloon at the same level but inflated with only 65 c.c. of air. Note the redevelopment of the changes noted in Fig. 2, *E*.**

balloon. Fig. 2,*F* is a tracing taken twenty minutes after 5.0 mg. of novatropine had been administered subcutaneously with the balloon at the level of the diverticulum and inflated to a pressure of 120 mm. of mercury.

Swallowing cold water produced changes similar to those induced by right carotid sinus pressure or inflation of the balloon at the level of the diverticulum (Fig. 4,*D*).

Observations Made Three Weeks After Digitalis Was Discontinued.—In these later observations, measured amounts of air injected into the bag of the Miller-Abbott tube by syringe were used because of its greater simplicity.

Repeated stimulation of the right carotid sinus produced no symptoms. The cardiac rate slowed from 100 to 75 beats per minute (Fig. 3,*B*).

The balloon, inserted to the level of the diverticulum and distended with 100 c.c. of air, produced no symptoms. There was slowing of the heart rate from 100 to 60 beats per minute (Fig. 3,*C*). The change in the P wave may be considered evidence of downward displacement of the seat of impulse formation from its usual site in the sinus node.

Observations Following the Intravenous Administration of 0.8 Mg. of Digitoxin.—Right carotid sinus pressure, one hour after administration of the digitoxin, produced mild vertigo and reduction in the heart rate from 90 to 37 beats per minute. The electrocardiogram showed downward displacement of the site of impulse formation (Fig. 3,*D*).

The balloon inserted to the level of the diverticulum and distended with 80 c.c. of air one hour after administration of the digitoxin produced mild vertigo. The heart rate was reduced from 90 to 37 beats per minute. The electrocardiogram again showed downward displacement of the site of impulse formation but no atrioventricular dissociation (Fig. 3,*E*).

Inflation of the balloon with 65 c.c. of air at the level of the diverticulum four hours after administration of the digitoxin produced marked vertigo, pallor, and a slow, irregular heart rate. The electrocardiogram revealed sinus depression, downward displacement of the site of impulse formation, and atrioventricular block.

Observations Following the Subcutaneous Administration of 1.0 c.c. of Adrenalin (1:1,000 Solution) Four Hours After the Digitoxin.—Stimulation of the right carotid sinus fifteen minutes after administration of adrenalin was associated with an increase in the heart rate from 100 to 150 beats per minute with a normal sinus mechanism (Fig. 4,*A* and *B*). Left carotid sinus stimulation immediately thereafter produced no significant change in the heart rate (Fig. 4,*C*). This is a single observation and is included because it is so unusual and because the patient displayed no noticeable increase in apprehension at the time of the test. The observations were not repeated with adrenalin because of substernal distress caused by the dosage employed.

Inflation of the balloon with 100 c.c. of air at the level of the diverticulum approximately twenty-five minutes after 1.0 c.c. of 1:1,000 solution of adrenalin

had been administered subcutaneously caused no appreciable slowing of the heart rate. There were a few multifocal premature beats of supraventricular and ventricular origin.

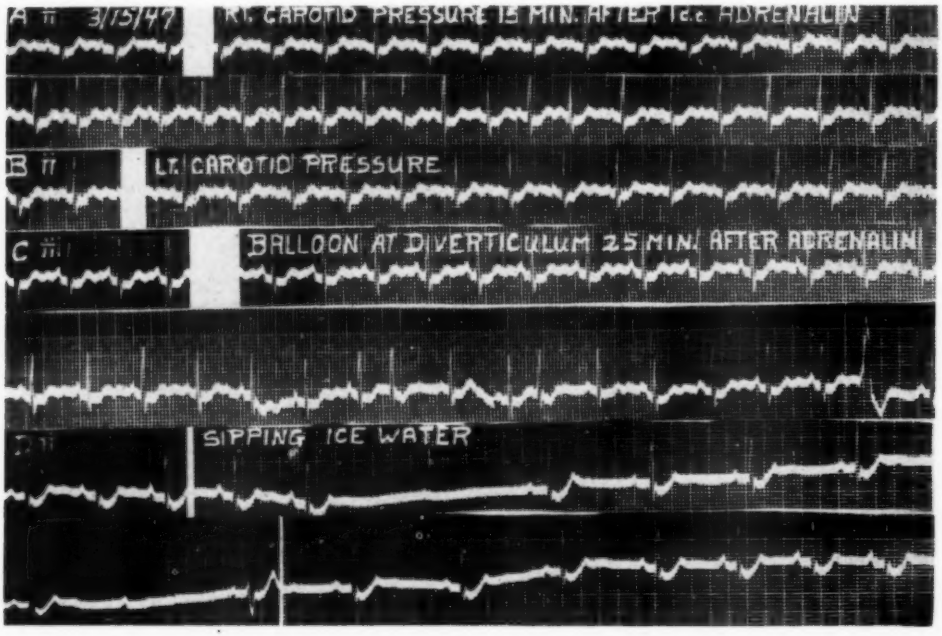

Fig. 4.—Electrocardiograms taken March 15, 1947, after completion of the observations in Fig. 3 and following the administration of 1 c.c. of 1:1,000 solution of adrenalin hydrochloride subcutaneously. The broad vertical lines indicate the point of stimulation or balloon distention.

A, Lead II showing the effect of right carotid sinus stimulation fifteen minutes after adrenalin. The two strips are continuous and show an increase in the sinus rate from 100 to 150 beats per minute.

B, Lead II taken immediately after *A*. Left carotid sinus stimulation had no effect upon the rate.

C, Lead II twenty-five minutes after adrenalin, with the balloon at the level of the diverticulum and inflated with 100 c.c. of air. There is no appreciable effect on the heart rate. A few supraventricular and ventricular premature beats may be noted.

D, Lead II taken March 20, 1947, while the patient was on a maintenance dose of digitalis. This shows the effect of sipping ice water. The two strips are continuous. Periods of sinus arrest, sinus slowing, and atrioventricular block are seen.

DISCUSSION

An extensive literature attests the interest shown in the various mechanisms responsible for the cardiac slowing or arrest producing the Adams-Stokes syndrome.

These conduction defects have been produced experimentally in animals or demonstrated in man in association with interruption of the anatomic integrity of the conduction system by congenital defect, trauma, gummata, various granulomata or other focal infectious lesions, tumors, necrosis, or fibrosis following myocardial infarction. At times the defect is physiological and reversible, the interruption being due to inflammatory lesions which resolve without tissue

destruction; rheumatic fever, diphtheria, and, less commonly, other infections have been implicated. Transient changes in the irritability of the conducting tissue have been demonstrated in asphyxia, after poisoning by various agents such as digitalis, quinidine, and strophanthus, in ischemia secondary to coronary insufficiency from any cause, and after cooling of the esophagus locally in the region of the auricles and junctional tissue. In a large group, reflex vagal stimulation is the important factor, the afferent portion of the reflex arc being by way of the cerebral, sympathetic, glossopharyngeal, or vagus nerves.

It appears likely that in many instances several of these factors operate concomitantly and frequently a summation of two or more is responsible for the development of conduction defects of sufficient degree to produce attacks. Such a summation effect was necessary to produce attacks in the patient described in this report. Digitalis in therapeutic or toxic doses did not produce spontaneous attacks but did sensitize the patient so that cardiospasm with resultant esophageal dilatation and distension of the esophageal diverticulum would produce spontaneous attacks. Artificial esophageal distention, the sipping of cold water, and right carotid sinus stimulation then produced minor clinical attacks with characteristic electrocardiographic conduction disturbances. It is possible that concomitant arteriosclerotic heart disease was an additional factor and by virtue of coronary insufficiency produced ischemia of the junctional tissue. The possible ischemic effect of coronary insufficiency, induced or aggravated by the coronary constrictor effect of vagal stimulation and digitalis, must also be considered.

Critical evaluation of the presence and relative importance of the many possible mechanisms is so difficult that one must be extremely cautious in ascribing the cause of the Adams-Stokes syndrome to any single factor. The possibility of multiple factors and their possible summation effect must always be considered. The disclosure of a surgically correctable source of a hypersensitive reflex in a patient with Adams-Stokes attacks may be a concomitant finding unrelated to the factor or factors producing the spontaneous attacks. This has accounted for some of the poor results from surgical treatment which we have seen. Before any surgical intervention is considered it must be shown that the reflex in question is responsible for initiating the spontaneous attacks, or is a summating factor associated with others which are incorrectable by such simple procedures as omission of a drug or resolution of an inflammatory lesion.

There are many unanswered questions in the problem of hyperirritable vagal reflexes which are raised again in these studies. The variation in tonus of the different autonomic reflexes in the same person in health or disease is poorly understood. The point of increased sensitivity of the reflex, whether sensory, central, or motor, is unsettled. The point or points of action of drugs such as digitalis in effecting the sensitivity of the reflex is not clear. The relation of carotid sinus hypersensitivity to arteriosclerosis is well recognized, but the reasons for this association are not clear. The effects of drugs or of the ischemia of arteriosclerosis may be central, on the motor endings, or on the conducting system itself. The hypersensitive reflex is then more apparent than real, a previously subeffective reflex becoming effective because of increased irritability

of the central nuclei or conducting system. Finally, the single observations on the effect of adrenalin are presented as a matter of interest with no attempt at explanation and no knowledge of whether repetition of the experiment would produce similar results.

CONCLUSIONS

1. A case of Adams-Stokes syndrome due to a vagovagal reflex induced by stimulation of an esophageal diverticulum is reported.

2. The summation effect of digitalis upon the vagovagal reflex and carotid sinus-vagal reflex necessary to produce the Adams-Stokes syndrome is described.

3. The probable frequency of multiple precipitating factors and their possible summation as the essential mechanism in the production of attacks is discussed.

4. Radical treatment should not be contemplated until easily corrected toxic or infectious causes have been eliminated. The reflex to be attacked radically must have been proved to be the sole precipitating factor, or the sole correctable summation factor, and not a concomitant reflex contributing no part to the spontaneous attacks.

5. Consideration of these possibilities will prevent certain of the surgical procedures which prove to be therapeutic failures.

REFERENCES

1. Nomenclature and Criteria for Diagnosis of Disease of the Heart, ed. 4, New York, 1946, New York Heart Association, p. 68.
2. Parkinson, J., Papp, C., and Evans, W.: The Electrocardiogram of the Stokes-Adams Attacks, Brit. Heart J. 3:171, 1941.
3. Weiss, S., and Ferris, E. B., Jr.: Adams-Stokes Syndrome With Transient Complete Heart Block of Vagovagal Reflex Origin. Mechanism and Treatment, Arch. Int. Med. 54:931, 1934.

Abstracts and Reviews

Selected Abstracts

Gilliatt, R. W.: Vaso-constriction in the Finger After Deep Inspiration. J. Physiol. **107**:76 (Jan.), 1948.

Reflex vasoconstriction after a deep thoracic inspiration has been reported by various investigators. It was the author's purpose to determine whether this response was initiated by a transient fall in blood pressure during the breath holding and mediated by the carotid sinus or some other pressoreceptor area. The work was carried out with a finger plethysmograph and a method of recording blood pressures continuously.

During a deep inspiration systolic pressure fell in all subjects, and then during the subsequent expiration a rise occurred which lasted for three or four heart beats. Following this there was a return to the control level. A diminution of finger volume invariably took place approximately three seconds after a deep inspiration.

The author concluded that inspiratory vasoconstriction was not a pressor reflex initiated by the fall in blood pressure which accompanied inspiration. However, he was unable to cast any light on the actual mechanism responsible for the reflex.

ABRAMSON.

Philipsborn, H. F., Jr., and Gibson, S.: Paroxysmal Tachycardia; Report of Two Cases Treated With Acetylcholine Bromide. Pediatrics **1**:205 (Feb.), 1948.

Two cases of supraventricular paroxysmal tachycardia in infants are presented. The authors obtained successful therapeutic results with digitalis in their previous ten cases with this type of arrhythmia. However, in Case 1, a 1-month-old infant, to a total dosage of 0.375 Gm. of Digifolin, given intramuscularly and intravenously, failed to stop the supraventricular paroxysmal tachycardia. When this patient was admitted to the hospital cyanosis, tachycardia, and enlargement of the liver to the iliac crest were striking. During digitalis therapy edema of the lower extremities appeared; the baby became comatose, and convulsions occurred. The intravenous injection of 1.0 mg. of acetylcholine bromide restored sinus rhythm a few seconds after the injection, and normal rhythm persisted until death occurred fourteen hours later as a result of extensive cerebral hemorrhage. The heart was normal.

An infant 3 weeks of age (Case 2) was well until three days before hospital admission when she cried out suddenly and became pale and cyanotic. When examined, she had a supraventricular paroxysmal tachycardia with a rate of 360 per minute and was thought to be moribund. Acetylcholine bromide was given intravenously in increasing quantities of 1.0 mg., 2.0 mg., and 4.0 milligrams. With the latter injection, sinus bradycardia followed by sinus tachycardia occurred and rapid improvement in the child's condition resulted.

Acetylcholine bromide is a powerful "parasympathomimetic" agent and must be used cautiously, with atropine sulfate ready for intravenous injection. It is not advocated in lieu of digitalis but only if digitalis fails to convert the arrhythmia to normal rhythm, or in urgent cases where immediate relief is indicated. The authors believe that this is the first report of the intravenous use of acetylcholine bromide in infants for the treatment of paroxysmal tachycardia.

JOHNSON.

Hanlon, C. R., and Blalock, A.: Complete Transposition of the Aorta and the Pulmonary Artery; Experimental Observation on Various Shunts After Corrective Procedures. Ann. Surg. **127**:385 (March), 1948.

The complete transposition of the aorta and the pulmonary artery is a relatively infrequent congenital anomaly. The condition in its pure form is described as the aorta arising from the right ventricle and the pulmonary artery from the left ventricle so that the systemic circulation and the pulmonary circulation are completely independent of one another. When no other abnormality is associated with this lesion, life is impossible. However, a number of anomalies, such as a patent interauricular septal defect, patent interventricular septal defect, and patent ductus arteriosus have been found in this condition in 123 cases. In this group, the average duration of life was nineteen months. These other defects make possible a mixture of blood between the right and left ventricles so that there is some oxygenation.

The authors considered various means by which this condition might be helped and carried out experiments in the dog in which the superior pulmonary veins are joined to the right auricle by suture in one group of animals and to the superior vena cava in another group. A special clamp which does not interrupt the main flow of blood through the auricle and superior vena cava is employed during the construction of the anastomosis. They found that the technical aspect of both procedures is not particularly difficult. However, in a group of ten dogs having anastomoses between the pulmonary veins and the right auricle, only four of the anastomoses were entirely satisfactory. In the other six, either marked constriction or complete occlusion occurred. On the other hand, when the pulmonary veins were anastomosed to the superior vena cava at the opening of the azygos vein in fifteen animals, thirteen survived for a sufficient length of time to make evaluation worth-while, and ten of these showed excellent results. Of the three failures, technical difficulties were experienced at the time of operation.

The authors conclude that "anastomosis of the pulmonary veins to the superior vena cava appears feasible in man and offers one possible approach to the surgical treatment of complete transposition of the great cardiac arteries."

LORD.

Arnott, W. M., and Macfie, J. M.: Effect of Ulnar Nerve Block on Blood Flow in the Reflexly Vasodilated Digit. J. Physiol. **107**:233 (March), 1948.

Although it has been settled that vasoconstrictor fibers leading to the skin are present in mixed peripheral nerves, the existence of comparable vasodilator fibers is still in doubt. In an attempt to elucidate this problem, the authors studied the reactions of the ulnar nerve in man. First they determined heat elimination from the distal phalanges of the fifth digits following abolition of vasoconstrictor tone by means of body heating; then they compared these results with those observed after both removal of vasoconstrictor tone and blocking of the ulnar fibers to the fifth digits with procaine. Ulnar block did not alter the heat elimination. Furthermore, the reduction in heat elimination produced by exposure of a reflexly vasodilated subject to a low environmental temperature was also not materially affected by ulnar blocking. From such evidence, the authors concluded that no specific nervous vasodilator activity is present in the ulnar nerve in man.

ABRAMSON.

Taussig, H. B.: Tetralogy of Fallot: Especially the Care of the Cyanotic Infant and Child. Pediatrics **32**:307 (March), 1948.

The purpose of this paper is to discuss the medical care of the cyanotic infant and the means of aiding an infant to survive until he is old enough to withstand operation. The ideal age for operation in patients with the tetralogy of Fallot is 5 to 9 years, when there is a 90 per cent chance of improvement as a result of surgical therapy. In infants the operative mortality is greatly increased and approaches 30 per cent. This operation should be postponed, if at all possible, until childhood.

Cyanosis may not be apparent for six months or longer if the ductus arteriosus remains patent. The initial complaint may be failure to gain weight, and these infants often present

difficult feeding problems. Small, frequent feedings may be helpful and cereals and vegetables in small amounts may be tolerated better than a large amount of milk. Episodes of severe paroxysmal dyspnea are common and are best treated by placing of the infant in the knee-chest position. If relief is not obtained immediately, morphine in dosage of 1.0 mg. per 5 kilograms of body weight should be given. This is almost specific for the relief of paroxysmal dyspnea due to inadequate blood flow.

It is important to remember that anemia may be present in these infants. With anemia the infant's color is less cyanotic but there is less available oxygenated hemoglobin and the oxygen carriage in the blood is greatly lessened. Infants with persistent cyanosis and moderately low red cell count may be helped with repeated small transfusions.

Adequate fluid intake is important in the presence of polycythemia because it lessens the danger of cerebral thrombosis. Infants should receive 800 to 1,000 c.c., children, 1,500 to 2,000 c.c., and adults, 2,500 to 4,000 c.c. of fluid daily. Since convulsions or severe headache may be a precursor of impending cerebral thrombosis, fluids should be forced in patients presenting such manifestations. If paresis or hemiplegia occurs, venesection and replacement by saline or glucose solution, oxygen therapy, and heparin therapy are indicated. With prompt therapy residual hemiplegia can be prevented in most instances.

If the number of episodes of paroxysmal dyspnea is lessening or if attacks can be relieved by the knee-chest position, there is less risk in the postponement of operation than in early operation.

JOHNSON.

Nichamin, S. J.: Stokes-Adams Syndrome Associated With Complete Congenital Heart Block in Infancy and Childhood. Pediatrics **32**:327 (March), 1948.

Stokes-Adams snydrome is an uncommon clinical condition in infancy and childhood. Syncopal attacks associated with bradycardia early in life should suggest congenital heart block. It is stated that a slow ventricular beat is essential for the Stokes-Adams attack, for as the diastolic pressure falls during the long interval between beats, there is a diminution in cerebral blood supply. The anoxia may be a factor in producing the convulsive disorder. The primary differential diagnosis is from idiopathic epilepsy. There is always the possibility of sudden death during the attack. Because of the anatomic anomalies of the conduction system in congenital complete heart block, drugs are probably of no value.

A case is reported of a child, first seen at 19 months of age, with a convulsion and a pulse rate of 40 beats per minute, who showed complete A-V heart block. The heart was enlarged and the hilar markings were prominent. The electroencephalogram was considered to be an unstable normal.

JOHNSON.

Lord, J. W.: Arterial and Venous Hypertensive States Benefitted by Surgical Intervention. Surgery **23**:550 (March), 1948.

The author points out that there are three hypertensive states which can be aided to a greater or lesser degree by surgical intervention. The first one, coarctation of the aorta, in favorable cases, can be returned to normal by removal of the stenotic segment and end-to-end anastomosis. The operation is tolerated well and the elevated blood pressure in the arms returns to normal and the low blood pressures in the legs rise to levels above those in the arms.

The second, essential and malignant arterial hypertension, is benefitted in the majority of cases by thoracolumbar sympathectomy, although only a small percentage of patients have normal blood pressures after operation. A significant reduction occurs in approximately 75 per cent of the patients operated upon. When careful selection of patients is carried out, the mortality as a result of the operation is extremely low.

The third condition which may be significantly aided by a variety of surgical procedures is that of portal hypertension, whether it is due to intrahepatic block of the portal vein (cirrhosis of the liver) or extrahepatic block of the portal vein (Banti's syndrome). Patients with portal hypertension frequently have massive gastrointestinal hemorrhage from esophageal varices.

The operation, when successful, lowers the pressure considerably in the portal system, which in turn improves the prognosis in this group of patients.

LORD.

Thompson, W. P., and Jellen, J.: Heart Size in Four by Five Inch Films. Am. Rev. Tuberc. **57**:379 (April), 1948.

One hundred ten individuals who were studied clinically were selected to represent small normal heart size, average normal heart size, and slight, moderate, and marked enlargement of the heart. In each individual, standard and miniature films were made in full inspiration. Miniature films made at a short target-film distance of about 43 inches introduce relative magnification of the heart, as compared with teleroentgenograms made at the usual distance of 72 inches. On the average, the transverse diameter of the heart was 3.701 times greater in the standard than in the miniature films; 3.7 is, therefore the conversion factor when comparison is made between the two techniques. The cases studied show that this method can be used as reliably for cardiac measurement as the standard 14 by 17 inch teleroentgenogram. The conversion factor of 3.7 may be used to multiply the transverse diameter found in 4 by 5 inch films made at a distance of 43 inches and the result then applied to the standard prediction tables in general use. Survey films are made during full inspiration while the tables generally apply to films made at the end of normal quiet inspiration. Thus, a heart which appears enlarged by the table will, in fact, almost certainly be enlarged.

A study was also made of the cardiothoracic ratio. When a cardiothoracic ratio of 50 per cent was accepted as the upper limit of normal, the correlation was not good. In ninety-nine cases in which the cardiothoracic ratio could be compared by the two techniques, both the table method and the cardiothoracic ratio agreed in indicating enlargement or lack of enlargement in seventy-seven cases. In the remaining cases one method indicated enlargement while the other did not. These authors admit that the use of the cardiothoracic ratio will omit a number of patients with cardiac enlargement and will lead to suspicion in a number of patients with normal hearts.

The conclusion is drawn that a diagnosis of heart disease may not be made on the basis of survey films alone, and that suspected cases should be studied clinically and by the use of standard 14 by 17 inch teleroentgenograms.

BELLET.

Hinton, J. W., and Lord, J. W., Jr.: The Selection of Patients for Thoracolumbar Sympathectomy. Ann. Surg. **127**:681 (April), 1948.

As a result of their clinical experience with 375 hypertensive patients undergoing thoracolumbar sympathectomies, the authors arrived at a group of principles or rules which enabled them to eliminate the majority of patients who were bad risks. In general, patients who show wide-spread, extensive involvement of the brain, eyes, heart, and kidneys should not be operated upon. Patients with persistent elevation of the blood urea nitrogen and nonprotein nitrogen because of marked impairment of renal function are also bad subjects for operation. A third group of patients manifesting mental confusion which seems to be on an organic basis prove to be poor risks. Finally, patients whose cardiac status is one of unremitting congestive failure should be rejected.

LORD.

Sciarini, L. S., Ackerman, E. M., and Salter, W. T.: The Response of Isolated Hypodynamic Myocardium to Inotropic Drugs. J. Pharmacol. & Exper. Therap. **92**:432 (April), 1948.

The authors used the papillary muscle from the right ventricle of a cat which was made to contract until weakened and then was subjected to small doses of ouabain so that the "therapeutic" effect of increasing its strength of contraction could be calibrated. This type of calibration differs from the standard assay methods in that the toxicity of the drug to be assayed does not

enter into the calibration and only positive inotropic effect of the drug is measured. Variable factors such as absorption, distribution, excretion, and destruction play no part in the calibration.

After calibration with a ouabain standard, each individual papillary muscle can be assigned its own muscle constant, a. Then the fractional response, R, to any glycoside, G, may be established by an equation:

$$\log G + \log M + \log a = 0.5 \log [R(1-R)]$$

where $\log M$ is the negative log potency of the glycoside.

GODFREY.

White, W. F., Belford, J., and Salter, W. T.: Isodynamic Equivalents of Digitoxin Cogenersas Tested on Hypodynamic Myocardium. J. Pharmacol. & Exper. Therap. **92**:443 (April), 1948.

Results obtained by the methods described in the preceding abstract (J. Pharmacol & Exper. Therap. **92**:432, 1948) were compared with the potency values assigned to various cardiac glycosides by the standard assay method (lethal effect on the intact cat).

The over-all results showed a surprising similarity, indicating that despite the obvious defects in the cat assay methods, the available data on the potency of the various cardiac glycosides are probably very nearly correct.

GODFREY.

Cauldwell, E. W., Siekert, R. G., Lininger, R. E., and Anson, B. J.: The Bronchial Arteries: An Anatomic Study of 150 Human Cadavers. Surg., Gynec. & Obst. **86**:395 (April), 1948.

In an extensive study of the bronchial arteries in 150 human cadavers, the authors found that there were essentially nine different types of bronchial arterial supply. In approximately 80 per cent the supply was represented by either one or two pairs of bronchial arteries arising from the descending aorta. In some instances as many as four bronchial arteries were found on the left side, whereas usually only one or two were found on the right. The mid-portion of the esophagus receives the major portion of its blood supply from the adjacent bronchial arteries.

LORD.

Shumacker, H. B., Jr., Speigel, I. J., and Upjohn, R. H.: Causalgia. II. The Signs and Symptoms, With Particular Reference to Vasomotor Disturbances. Surg., Gynec. & Obst. **86**:452 (April), 1948.

Causalgia follows partial injury of peripheral nerves and is characterized by a burning type of pain, associated with signs of emotional instability and irritability, nutritional changes, and either vasoconstriction or vasodilatation in the affected limb.

The authors present their findings in a group of ninety male patients suffering from this condition. In every instance one or more of the major nerves to the extremities were injured. In almost all of the cases pain was burning in character, although frequently associated with other types of discomfort. Almost without exception the pain was made more intense by the use of the part or by tapping or touching the affected hand or foot. Placing the limb in dependency aggravated the condition. In all instances the symptoms were localized in the hand or foot, and it was commonly limited to, or was more intense in the distribution of the injured nerve.

Of the number on whom skin temperature studies were done, in about one-third the digits of the affected hand or foot were almost equal in temperature to those of the opposite normal side. In approximately one-fifth of the patients the involved limb was colder than the other. In the remainder the digital skin temperature of the injured extremity was distinctly higher than that of the other. It would seem, then, that the pain was unrelated to the state of vasomotor tonus, since it was experienced in the presence of increased, decreased, or relatively normal vasomotor tonus.

ABRAMSON

Fowler, N. O., Jr., and Failey, R. B., Jr.: Perforation of the Infarcted Interventricular Septum; Report of Two Cases, One Diagnosed Ante-mortem. Am. J. M. Sc. **215**:534 (May), 1948.

Including the authors' two cases, a total of fifty-six cases of infarcted interventricular septum with perforation have been found in the literature; fifteen of these were diagnosed ante mortem. In thirty-eight patients whose survival time was known, thirty-one survived less than one month, thirty-seven less than one year, and one survived four years and ten months. Forty-three patients of forty-five examined showed systolic murmurs, usually maximal to the left of the lower sternum; twenty-two showed systolic thrills; only three showed diastolic murmurs.

The diagnosis should be suspected in any patient known to have a myocardial infarction who suddenly develops a systolic murmur and thrill to the left of the lower sternum. The only condition likely to be confused is rupture of a papillary muscle following cardiac infarction. In this condition the murmurs are louder and nearer the apex, and the ensuing failure is left-sided rather than right-sided.

DURANT.

Baer, S., Heine, W. I., and Gelfond, D. B.: The Use of Vitamin E in Heart Disease. Am. J. M. Sc. **215**:542 (May), 1948.

Early in 1946 attention was called by Vogelsang and Shute to the marked improvement resulting from the administration of vitamin E to patients with various forms of heart disease. Considerable publicity was given to the phenomenal therapeutic results claimed in congestive heart disease and angina pectoris by these authors. Shute was quoted as saying: "We have not learned of a single failure. The percentage of success is remarkable." Patients began to request this treatment from physicians, and less scrupulous drug houses, in their attempts to sell preparations of alpha-tocopherol, quoted entire paragraphs from the articles recommending vitamin E.

The authors began their study of vitamin E in heart disease in August, 1946, and their report includes observations on twenty-two patients. Doses of 300 to 400 mg. daily were given to eleven patients with congestive heart failure, five patients with angina pectoris, and six patients with hypertensive and, or arteriosclerotic heart disease. In no case was there any demonstrable effect on the electrocardiogram, orthodiagram, or blood pressure. None of the twenty-two patients was markedly or moderately improved. Six patients were questionably improved, and the remainder showed no change or became distinctly worse. The results are so at variance with those published that the authors hesitate to recommend the use of vitamin E in heart disease. Certainly much more scientific work must be done in this field before suggestions are made that so appreciably alter our present forms of cardiac therapy.

DURANT.

Hinchley, J. J., Hines, E. A., Jr., and Ghormley, R. K.: Osteoporosis Occurring During Potassium Thiocyanate Therapy for Hypertensive Disease. Am. J. M. Sc. **215**:548 (May), 1948.

Osteoporosis with arthralgia was noted in 2 per cent of patients receiving potassium thiocyanate therapy for hypertension. Of eleven such patients, the age ranged from 46 to 68 years. There were six women and five men. Onset of symptoms associated with the osteoporosis generally occurred within three to six months after administration of the drug was started. They consisted of (1) pain on use of the extremity which began insidiously and gradually increased in severity, and (2) subsequent mild swelling of the joint or joints involved, but with no acute inflammatory reaction. The severe cases simulated those of extensive post-traumatic osteoporosis. Roentgenograms, which were limited to the involved regions, revealed mild to marked diffuse osteoporosis. No similar syndrome was found in more than 5,000 consecutive cases of hypertension in which this drug was not used.

Evidence at hand seems to suggest slight and prolonged interference with calcium metabolism as a possible mechanism for production of the syndrome. It appears that adequate calcium intake should be assured for persons who are taking potassium thiocyanate. Use of this drug may be contraindicated in the presence of bone malacia, such as senile osteoporosis or osteitis deformans;

likewise its use may be inadvisable in the presence of fracture, not with regard to union of the fracture, but because any interference with calcium metabolism in the presence of increased calcium requirement might precipitate osteoporosis.

DURANT.

Harman, J. W.: The Significance of Local Vascular Phenomena in the Production of Ischaemic Necrosis in Skeletal Muscle. Am. J. Path. **21**:625 (May), 1948.

As a sequence to his previous work on the nature of the ischemic degeneration of skeletal muscle, Harman studied the vascular phenomena associated with both acute and necrotic ischemic necrosis of skeletal muscle. In discussing the classical clinical studies on this problem by Volkman down to Leriche, the author notes that arterial and venous lesions and vascular spasm have been considered the major factors without any consideration of capillary function which is so important in skeletal muscle. It is particularly important because of the unique gradient of permeability in muscle capillaries.

Harman produced complete ischemia in the right hind legs of rabbits by use of tourniquets. This was proved by the failure of Fluoresite injected intravenously to pass distal to the tourniquet. Angiography was employed on animals thus made locally ischemic for four to four and one-half hours; also after release of the obstruction at periods varying from three to forty-eight hours. Thorotrast and India ink were used, the animals being sacrificed within a few minutes and their extensor and flexor muscles excised from both the normal and ischemic legs. Tissue from both groups was fixed in formalin, then cleared by the Spalteholz method for direct visualization of injected vessels. Angiography consisted of two successive injections, 5 c.c. each of Thorotrast, quickly followed by x-ray exposure, a third exposure being made one minute after completion of the last injection.

Regardless of the duration of the ischemia, the pulse in the great saphenous artery was always palpable on release of the tourniquet. It became less palpable with the accumulation of edema fluid, but it was never obliterated. Angiography verified this continuous postobstruction arterial patency. In ten animals it also showed a definite sequence of visualization. The veins of the ischemic leg would fill but this always was delayed, showing that the retardation was between the arteries and the veins, namely, in the capillary and fine venule sector. India ink injections used as a control showed penetration as far as the small intramuscular arterial branches.

Harman then injected bromphenol blue into one group of rabbits with ischemic right hind legs five minutes after release of the tourniquet. The rabbits of this group were studied one-half hour, three hours, and twenty hours after dye injection, with the muscles of both the ischemic and the normal hind legs exposed for direct visualization. When ischemia had lasted for four hours or longer, passage of dye through the damaged muscles was delayed in both its inception and completion. In the same study applied to a second group of rabbits, in which the dye was injected twenty hours after the release of the tourniquet, the results were strikingly emphasized, all being indicative of a functioning but sluggish intramuscular circulation.

The histologic picture of muscle several hours after the release of vascular obstruction showed profuse infiltration of monocytes and neutrophiles, edema, and various types of extensive degeneration of the muscle. The capillaries were dilated and nonthrombosed, but tightly packed with erythrocytes. The larger arterial and venous channels remained unaltered.

By determination of the weight of the excised muscles from both the ischemic and normal limbs, Harman demonstrated a significant increase in weight, due to edema, most marked in flexor muscles as contrasted with the extensors.

This experimental work was extended to permit observation on the muscle changes as late as fifteen to twenty days following release from ischemia. At this time injection of bromphenol blue revealed late sequelae which were the intense dye staining in shrunken but firm elastic and contractile muscles, weighing less than normal, but free of infarction, all of this in muscles subjected to ischemia for three hours or less. Muscles rendered ischemic for four hours or longer weighed more, contained yellow areas of infarction of variable size, and were electrically nonirritable.

The author points out that these changes differ greatly from those produced by venous occlusion and are similar to those produced by arterial occlusion, yet they occur in the presence of functionally preserved large arteries. He concludes that capillary damage is the basis for the ischemic necrosis of skeletal muscle, especially of the type leading to Volkmann's contracture, and draws an analogy between this and the experimental work of Meneely which showed that abnormal capillary permeability permits progressive myocardial destruction after release of temporary coronary artery occlusion.

This extensive experimental work conclusively removes venous obstruction as a factor in the pathogenesis of ischemic muscle necrosis, yet does not decisively differentiate between arteriolar and capillary damage, a fine point of distinction which may have pharmacologic and therapeutic implication in future studies on this subject.

GOULEY.

Ganem, E. J., and Cahill, G. F.: Pheochromocytomas Coexisting in Adrenal Gland and Retroperitoneal Space, With Sustained Hypertension. New England J. Med. **238**:692 (May 13), 1948.

A case of coexisting intra- and extra-adrenal pheochromocytomas in a 12-year-old girl is reported. Profuse sweating, heat intolerance, excessive appetite without weight gain, excessive thirst, fatigue, palpitation, and paresthesias of the hands had been noted for about two years. On examination, undernutrition, emotional instability, warm and moist skin, and tachycardia were found. The blood pressure averaged 180/120 and the pulse, 120 per minute. In the laboratory studies, the basal metabolism ranged from +51 to +67 per cent. The blood iodine was normal. During a nine months' period of observation, the blood pressure rose to 200/150 and papilledema appeared. Lugol's solution was not helpful.

Left adrenal enlargement was then demonstrated by bilateral perirenal air insufflation after urography had shown no abnormality. Improvement followed removal of an intra-adrenal pheochromocytoma. A second tumor mass was suspected at operation, but was not removed. The blood pressure remained pathologically elevated.

It was considered probable that pathologic tissue was still present. This impression was supported by the prompt reduction in blood pressure which followed the intravenous administration of a benzodioxane (1164F). At a second operation, a second tumor was removed from the left retroperitoneal space. Complete recovery followed convalescence. The blood pressure fell to normal and was thereafter not influenced by the injection of 1164F.

Variations in the clinical manifestations of pheochromocytoma are discussed. Importance is placed on perirenal insufflation of air as an aid in the localization of early enlargements of the adrenal gland. The value of nontraumatic surgical technique and of careful administration of adrenalin and adrenal cortical extracts during and after operation is stressed.

KAY.

Hodge, G. B., and Messer, A. L.: The Electrocardiogram in Biliary Tract Disease and During Experimental Biliary Distention: Clinical Observations in 26 Patients. Surg., Gynec. & Obst. **86**:617 (May), 1948.

The authors studied the effect on the electrocardiogram of distention of the gall bladder and common duct in twenty-six patients with biliary tract disease during the procedure of removal of the gall bladder and postoperatively in cases of common duct exploration by means of the T tube. They noted in patients with normal cardiovascular systems that there were changes in the electrocardiogram in some patients during anesthesia; in others, during the operation. None of these changes suggested myocardial insufficiency. Distention of the gall bladder to a pressure of 100 cm. of water caused an increase in the pulse rate and blood pressure of some patients, whereas in others a decrease occurred. Postoperatively, distention of the common duct by injection of a saline solution to a pressure of 100 cm. of water caused pain in the epigastrium and occasionally pain radiating to the back, but never did the pain simulate that of angina.

The authors conclude that there is no definite electrocardiographic pattern in gall bladder disease and that the changes which occur are variable and are probably coincidental.

LORD.

Adams, H. D.: Surgery of the Major Blood Vessels. Texas State J. Med. 44:10 (May), 1948.

A number of vascular disorders affecting the major vessels lend themselves to treatment by surgical methods. The simplest of these is peripheral arterial embolism. Success in the surgical treatment of this condition depends upon early recognition and immediate embolectomy. Generally approximately one-half of the patients will be saved if this procedure is performed within ten hours after occlusion of the vessel has occurred, while after thirty hours none will be saved. Commonly the embolus will lodge at the various bifurcations of the main vessels. It is necessary not only to remove the embolus, but an attempt must be made to suck out the distal thrombus and establish free back flow of blood and a return of normal arterial pulsations in the peripheral vessels.

Arteriovenous aneurysms of the peripheral arteries are most readily treated by quadruple ligations and excision of the involved segments. This procedure can be carried out in almost any major artery of the body except possibly the carotid and the popliteal arteries. The objection to performing the operation on the carotid artery is the high incidence of cerebral damage which follows, while in the case of the popliteal, generally gangrene of the foot will occur because of the poor collateral circulation around the knee.

In the case of arterial aneurysm, the artery and also the accompanying vein are ligated and the false sac is removed. This method appears to have certain advantages over any type of plastic procedure.

Aside from surgery of the major vessels of the extremities, recently great strides have been made in applying similar principles to the large vessels in the chest. Since a patent ductus arteriosus usually causes death at an early age from congestive heart failure or subacute bacterial endocarditis, attempts have been made to treat the condition surgically by active division of the connecting vessel between aorta and pulmonary artery. Similarly, coarctation of the aorta has been cured either by means of an anastomosis between the proximal divided end of the left subclavian artery and the site of the aorta distal to the coarctation or by end-to-end anastomosis of the aorta after the stenosed portion has been removed. In the case of pulmonary stenosis, the formation of an aortopulmonary fistula or the production of an anastomosis between the right or left subclavian artery with the corresponding pulmonary artery has led to considerable change in the clinical appearance of the patient.

For the relief of symptoms of portal hypertension, it is necessary first to determine whether hepatic or extrahepatic portal obstruction exists. In the intrahepatic type, impaired hepatic function can be demonstrated by the various clinical tests. Gastrointestinal hemorrhage, ascites, or both, or the classical clinical syndrome of Banti's disease are the primary indications for surgical intervention. If there is hypertension in the splenic vein and not in the inferior vena cava, splenectomy and splenorenal anastomosis are effective in stopping the gastrointestinal hemorrhages. If intrahepatic block or extrahepatic portal block high in the liver is present, a portocaval anastomosis or Eck fistula can be carried out.

ABRAMSON.

Nygaard, K. K.: Intermittent Raynaud's Phenomenon Resulting From Nonunited Fracture of the Navicular Bone. Am. J. Surg. 75:834 (June), 1948.

The author reports a case of Raynaud's phenomenon in a patient with a nonunited fracture of the navicular bone. Initially the lesion had been treated with a plaster cast which had been worn for three weeks. For several years after the accident, the patient complained of moderate pain in his hand. Subsequently this increased in severity. At the same time the patient noted that when he performed certain functions involving the affected hand, he would develop a tingling sensation and weakness of the muscles of the hand. Generally associated with these symptoms were episodes of Raynaud's phenomenon involving the fingers. The attacks were not related to a cold environment nor were they precipitated by worry or anxiety. Examination revealed a bony, hard, irregular prominence over the navicular bone which by x-ray was shown to be related to a transverse nonunited fracture of this bone. Following operative interference, the local tender-

ness disappeared and the procedures previously producing the episodes of Raynaud's phenomenon were now no longer effective in this regard.

It is the author's opinion that during weight carrying the pain associated with the impingement of the loose fragments of the navicular bone against the nerve endings in the adventitia of the radial artery was in some way related to the initiation of the Raynaud's phenomenon.

ABRAMSON.

Levy, H., and Boas, E. P.: Vitamin E in Heart Disease. Ann. Int. Med. **28**:1117 (June), 1948.

Thirteen patients were treated with alpha-tocopherol, the daily dosage varying from 200 to 800 milligrams. In most of the patients, plasma levels of alpha-tocopherol were determined while the vitamin was being taken; in some, control levels were also taken before the vitamin was administered. Four of the patients with chronic heart failure responded dramatically to a low-salt diet after large doses of vitamin E had caused no diuresis or improvement in the state of heart failure. There was no evidence whatsoever that this drug affected the pattern, the frequency, the intensity, or the precipitation of anginal pain in five patients with chronic anginal pain with a stable pattern of chest pain related to effort. Likewise, in three cases of angina pectoris, in states of coronary insufficiency characterized by a new pattern of increased frequency and intensity of attacks, often occurring at complete rest, there was no change to be attributed to the use of this vitamin.

WENDKOS.

Caldwell, H. W., and Hadden, F. C.: Carotid Artery Thrombosis: Report of Eight Cases Due to Trauma. Ann. Int. Med. **28**:1132 (June), 1948.

During World War II, the ante-mortem diagnosis of post-traumatic thrombosis of a carotid artery was substantiated in six soldiers either at necropsy or at the time of operation. The condition was suspected during life because of the occurrence of various types of paralysis following penetrating or nonpenetrating injuries to the neck. The diagnosis in two other patients who presented similar features during life was established only at necropsy. Recovery in one case was apparently due to the early institution of heparin therapy after the clinical diagnosis was made. The neurological findings are explained by cephalad propagation of the thrombus with resultant occlusion of the external carotid and the branches of the internal carotid including one-half of the circle of Willis, or else by embolism by fragments of the thrombus to the smaller cerebral vessels.

Surgical occlusion of the vessel and possible resection above and below the thrombus is possible if carried out early. The absence of the temporal pulse on the involved side is good confirmatory evidence that the common carotid and possibly the external carotid is occluded. This sign is of value also in indicating to the surgeon the extent to which the carotid vessel must be dissected if surgery is the elected type of therapy. The absence of the right radial pulse may indicate that the subclavian artery is also occluded by the thrombus propagating toward the heart.

It is suggested that exploration of the carotid vessels at autopsy may demonstrate the true etiology of some obscure cases of "apoplexy."

WENDKOS.

Hollander, G., and Mandelbaum, H.: The Treatment of Angina Pectoris With Propylthiouracil. Ann. Int. Med. **28**:1150 (June), 1948.

Ten hypertensive patients with a definite anginal syndrome varying in duration from five months to seven years were treated with 6-propylthiouracil in doses up to 200 mg. a day. Only one of the ten patients was male. The ages of the patients varied from 45 to 62 years. Symptomatic improvement occurred in four cases for a six-month period. The initial basal metabolic rate and the subsequent readings did not determine the final results. Myxedema levels were not necessary for relief of pain since three of the four patients who were relieved of pain had basal metabolic rates within normal limits at the time symptoms were improved. If improvement

did occur, it did so within eight weeks of beginning treatment. The observed, untoward effects of 6-propylthiouracil were a tendency to water retention and intermittent claudication. No toxicity with 6-propylthiouracil, in doses up to 200 mg. a day, was observed.

WENDKOS.

Barden, R. P., and Cooper, D. A.: Peripheral Vascular Disease in the Lungs: Roentgenologic Manifestations. J. A. M. A. **137**:584 (June 12), 1948.

The authors review the various disorders which affect the peripheral pulmonary vessels and which may produce roentgenographic changes. The diseases are classified under three categories: (1) Intrinsic disease of the vessel wall (arteriosclerosis and arteriolosclerosis) or obstruction of the vascular lumen (embolism by clot, neoplastic cells, and parasites, and thrombosis, as seen in the leucemias and polycythemia vera). The close association between obliterative vascular changes and pulmonary hypertension, and between obliterative vascular disease and pulmonary emphysema is pointed out. (2) Vascular change secondary to disease of the adjacent parenchyma (acute and chronic pulmonary inflammatory disorders, and neoplasms of the lung). (3) Toxic and hypersensitivity states (sulfonamide poisoning, serum sickness, acute rheumatic fever, lupus erythematosus, periarteritis nodosa, glomerulonephritis, hypoproteinemia, beriberi).

These disorders all bring about increased permeability of the pulmonary capillaries with consequent patchy or massive edema and present the same type of roentgenologic picture.

HANNO.

Peet, M. M., Isberg, E. M., and Bassett, R. C.: Toxemia Superimposed Upon Prepregnant Hypertension Treated by Splanchnicectomy. Surg., Gynec. & Obst. **86**:673 (June), 1948.

The authors point out that about 50 per cent of prepregnant hypertensive women can be expected to develop a superimposed toxemia and that one-fourth of these patients are left with higher blood pressure levels and more extensive disease as a result of a toxemic pregnancy. The authors report five patients with hypertension who developed a toxemia during pregnancy. Each of these patients was submitted to bilateral supradiaphragmatic splanchnicectomy with excellent results, including return to normal levels of the blood pressure and relief of the toxemia in two patients. These two patients also continued to do well as long as four years and two years, respectively, after operation. Of the three remaining patients, two were helped moderately and one was a failure. The failure occurred in a patient who exhibited extremely poor renal function and who subsequently died fifteen months after operation.

In the discussion, the authors point out that splanchnicectomy should be performed within the first three weeks of the toxemia in this group of patients. Further, if splanchnicectomy has not relieved the toxemia within three weeks, then the pregnancy should be terminated. The third point made by the authors is that splanchnicectomy should not be employed in patients whose toxemia of pregnancy is associated with marked renal damage.

LORD.

Kiesewetter, W. B., and Schmacker, H. B., Jr.: An Experimental Study of the Comparative Efficacy of Heparin and Dicumarol in the Prevention of Arterial and Venous Thrombosis. Surg., Gynec. & Obst. **86**:687 (June), 1948.

In an extensive series of experiments carried out on dogs, the authors developed a technique of effecting thromboses in veins and arteries with great consistency. Approximately 90 per cent of the veins (jugular and femoral), 80 per cent of the small arteries (femoral), and 70 per cent of the large arteries (carotid) were thrombosed by the seventh day following trauma in control animals. In the group treated with heparin a significant reduction in the incidence of thrombosis was noted: 56 per cent of the veins, 6.7 per cent of the small arteries, and 9.5 per cent of the large arteries. In the Dicumarol-treated animals, the incidence of thromboses was 41 per cent of the veins, 50 per cent of the small arteries, and 15.8 per cent of the large arteries.

The authors conclude that anticoagulant therapy is of great value in the prevention of thromboses of veins and arteries subsequent to trauma. However, with the possible exception of the superiority of heparin in the prevention of thrombosis of injured small arteries, the difference between the anticoagulants, heparin and Dicumarol, was not significant.

LORD.

Elkin, D. C., Cooper, F. W., Jr., Rohrer, R. H., Miller, W. B., Jr., Shea, P. C., Jr., and Dennis E. W.: The Study of Peripheral Vascular Disease With Radioactive Isotopes. Part I. Surg., Gynec. & Obst. **87**:1 (July), 1948.

The authors utilized radioactive sodium 24 in the investigation of the circulation to the extremities. Two methods were studied. In one, 5 c.c. of the prepared solution was rapidly injected into an antecubital vein and the circulation time to the lower extremity was determined by noting the sudden rapid increase in the rate of count of the Geiger-Mueller detector placed posterior to each gastrocnemius muscle and at the ball of each foot. The figure obtained depended not only upon the flow of blood to the part but also upon the diffusion of sodium chloride from the vessel into the extravascular spaces. The second method consisted of injecting the sodium directly into the gastrocnemius muscle and determining the rate of disappearance of the material as recorded on a detector placed behind the gastrocnemius muscle. The rate of removal depended upon the circulation through the nutrient capillaries.

It is the authors' opinion that with this procedure a means is at hand for determining the relative blood flow to the muscles, since the rapidity of removal of the sodium from this tissue is related to the volume of blood flow locally.

ABRAMSON.

Puddu, V., and Mussafia, A.: Considerations on the Electrocardiogram During Exercise Tests. Acta Cardiol. **2**:140, 1947.

Depression of the RS-T segment during exercise in patients with coronary artery disease may be explained by a delay of endocardial repolarization. Occasional elevation of the RS-T segment must be assumed to be the result of a diffusion of the ischemic region toward the epicardial layers. Uprighting of a previously inverted T wave during the test is explained as the result of a balance between two regions, one of which is characterized by delay of repolarization at rest, the other by a normal resting condition which upon exercise becomes equally delayed. A temporary "normalization" of the record must result.

HECHT.

Segers, M.: Interaction Between Auricles and Ventricles. Acta Cardiol. **2**:335, 1947.

Three clinical examples are presented in which an interaction between auricles and ventricles could be demonstrated in the presence of complete A-V block. The presence of such interaction in the apparent absence of anatomical pathways may be seen (1) in synchronization of auricular and ventricular beats in instances of complete A-V block; (2) in shortening of P-P intervals in complete A-V block during the ventricular excitation; (3) in alteration of the contour of the P wave in complete block in auricular beats that follow the ventricular complex; (4) in auricular extrasystoles appearing in close relationship to the ventricular beats in A-V block; and (5) in an abnormal duration of the ventricular compensatory pause after ventricular extrasystoles. No physiological explanation has been attempted.

HECHT.

Wallgren, A.: Tuberculous Heart Disease. Acta med. Scandinav. (Suppl.) **196**:132, 1947.

Three cases of tuberculous pericarditis are reported. The first, an 8-year-old boy, died of exudative and adhesive pericarditis following fever, erythema nodosum, and a left hilar lesion with enlarged retrocardiac nodes. A left upper lobe caseous pneumonia was found adherent to the pericardial surface. In contrast to this, two boys, 9 and 6 years of age, respectively, developed friction rubs, enlarged cardiac shadows, and altered T waves one month after the onset of febrile

primary tuberculosis of the lung. The cardiac signs persisted about three weeks and were accompanied by increased fever and further elevation of the sedimentation rate. There were no demonstrable cardiac sequellae except a change in the contour of the right auricular border in one boy. This was attributed to a pericardial adhesion. No rheumatic manifestations were recorded in the past histories, nor did any appear for the duration of a three-year follow-up period after the pericarditis. The author compares the situation in his latter two patients with acute "tuberculous-allergic" serofibrinous pleurisy on the basis of the brief course and good prognosis.

SAÏEN.

Graf, W., Moller, T., and Mannheimer, E.: The Continuous Murmur. Acta med. Scandinav. (Suppl.) **196:**167, 1947.

Phonocardiographic records in five frequency ranges were recorded simultaneously with Lead II of the electrocardiograph to demonstrate the characteristics and points of maximal intensity of the main types of continuous murmurs: in patent ductus arteriosus, the thyroid murmur of Graves' disease, arteriovenous aneurysm, the fontanel murmur of infants, and the venous hum of children.

The murmur of patent ductus arteriosus began about 0.04 seconds after the first heart sound. The regularity with which it was loudest in the second left intercostal space is stressed, the authors believing that continuous murmurs with their greatest intensities in the third and fourth intercostal spaces or the aortic area indicate other types of anomaly. Three pre- and postoperative phonocardiograms of patients with patency of the ductus arteriosus are reproduced, as well as tracings of a patient thought at operation to have a persistent truncus communis. The continuous murmur in this latter instance was loudest in the third left intercostal space.

The thyroid murmur was studied in thirteen women with Graves' disease and found to have a frequency extending up to 400 to 500 cycles per second. There was frequently a difference in intensity between the two lobes.

Three cases of arteriovenous aneurysm were studied, two intracranial and one at the ankle. The frequencies ranged between 500 and 1000 cycles per second.

One tracing of a fontanel murmur was reproduced. It was recorded both at the anterior fontanel and the external auditory meatus, and was of moderate amplitude in all frequencies between 50 and 500 cycles per second. It was believed to have been produced in the intracranial veins.

The venous hum in the neck was studied in forty children selected from 250 children examined. The incidence of the hum was 42.8 per cent from birth to 3 years, 65.5 per cent between 3 and 6 years, 52.9 per cent between 6 and 9 years, 47.8 per cent between 9 and 12 years, and 30.8 per cent between 12 and 15 years. The intensity was equal on both sides in one-half the cases studied, the remaining half being divided about equally between right and left sides as to maximal intensity. Turning the head to the opposite side increased the intensity of the murmur, as did deep inspiration, while digital compression of the jugular vein made it disappear. These characteristics were illustrated by tracings. The frequency range was 50 to 500 cycles per second but usually was not greater than 400 cycles per second.

SAÏEN.

Akesson, S.: Arterial Orthostatic Anemia With Cardiac Pains. Acta med. Scandinav. (Suppl.) **196:**192, 1947.

The author reports a 21-year-old man who developed vague and variable precordial pain and palpitation which became gradually worse for eighteen months and were related to exertion, anxiety, and eating. The blood pressure in recumbency was found to be 135/90 and the pulse, 80 per minute. After the patient had stood for eight minutes, these figures were, respectively, 115/85 and 104 per minute. The heart was normal by fluoroscopy. The electrocardiogram when the patient was recumbent showed slightly low T waves in the limb leads and a slightly diphasic T wave over the left precordium with a rate of 75 per minute. When the patient stood, marked T-wave inversion appeared in all leads, with 1.0 mm. of RS-T segment depression at a rate of 120 per minute. Breathing a mixture of 6.7 per cent oxygen and 4.5 per cent

carbon dioxide produced a similar electrocardiographic picture after fifteen minutes, though the abnormality was slightly less marked (rate, 130 per minute). The patient could perform violently exerting tasks although he felt precordial pain after about five minutes. He was hospitalized and a duodenal ulcer was found. It healed uneventfully, but without alleviating his pain, which became more frequent and radiated to his neck and his left arm. It was felt that Buerger's disease, juvenile arteriosclerosis, and myocarditis could be excluded with reasonable certainty. The patient was finally placed in a "sanitorium for neurotics."

The author comments on the infrequency of cardiac pain with postural hypotension, the significance of the positive anoxemia test, and the possibility of true myocardial damage having gradually been produced by recurrent postural hypoxic episodes.

SAŸEN.

Chini, V.: Clinical Aspects of the Associated Coronary and Cerebral Syndrome. Settim. Med. **35**:443, 1947.

The author studied the frequency and types of various cerebral disturbances which may follow myocardial infarction. This clinical picture has been called "cerebral type of myocardial infarction"; the author refers to it as "associated coronary and cerebral syndrome."

Myocardial infarction may be followed by restlessness, mental confusion, stuper, loss of consciousness, coma, syncope, or epilepsy. The neurological signs may be preponderant, and occasionally mask the main symptoms of the disease.

The author reports thirty clinical cases which are divided into four groups:

Group 1 includes patients with coronary and cerebral episodes which are definitely independent. The only connecting link is the existence of arteriosolerosis in both the heart and the brain. Group 2 includes patients with a neurological syndrome which masks the main coronary disturbance. Group 3 includes patients with angina pectoris and episodes due to functional disturbances of the cerebral vessels. Group 4 includes patients having a coronary occlusion which was followed after a short period by cerebral disturbances.

The cerebral phenomena may be due to the following causes: embolism, thrombosis, hemorrhage, cerebral anoxemia caused by low blood pressure, shock, vascular reflexes, edema of the brain, or anatomical lesions existing before the coronary attack. More than one factor may be operative in these episodes.

Whenever a focal syndrome is present, either embolism or thrombosis should be considered as the cause. A sudden occurrence is in favor of embolism, while a gradual occurrence is more common in thrombosis. The absence of thromboendocarditis at necropsy is in favor of cerebral thrombosis.

LUISADA.

Barsoum, G. S., Kenawy, M. R. and El-Sheehy, A.: Absorption of Khellin and its Estimation in Blood and Tissues. J. Roy. Egyptian M. A. **30**:312 (June), 1947.

The authors undertook to investigate the rate of the absorption of khellin after its administration by different channels and to determine the concentration which khellin reaches in the blood and tissues in animals and man. Khellin is extracted from blood or tissue by alcohol and chloroform. The concentration of this drug is determined by the modified colorimetric method of I. R. Fahmy or it is dissolved in Tyrode's solution and assayed by the biological method on the rectal cecum of the fowl (Anrep, Barsoum, Kenawy, and Misrahy 1946; Anrep, Kenawy, Barsoum, and Riad Fahmy, 1947) With concentrations of khellin in the blood varying between 1.0 and 200 micrograms per cubic centimeter, the plasma or serum contains about 10 to 20 per cent more khellin than the red blood cells. The authors found that khellin is readily given off by the corpuscles when they are exposed to serum or to Tyrode's solution containing no khellin; therefore, khellin in the red blood corpuscles is not pharmacologically wasted.

The experiments with intravenous injections of khellin were made on anesthetized dogs. The arterial blood pressure was recorded in the carotid artery and the injections were made slowly so as not to cause a fall of the blood pressure. After an intravenous injection the concentration of

khellin in the blood reaches a very high level for a short time. Within a few minutes the khellin concentration diminishes, and in about 30 to 40 minutes it reaches a steady level which is maintained for several hours. The rapid diminution of the khellin concentration in the circulating blood is due to its gradual and more or less uniform distribution among all the tissues of the body.

After intramuscular injection, khellin is extremely rapidly absorbed into the general circulation, and its concentration soon reaches a steady level, at which it is maintained for a long time. Maximal concentration reached after intravenous injection is much higher than after intramuscular injection of the same dose. Diminution of khellin in the circulating blood is not due to its elimination by the kidneys in an unchanged form. Since khellin remains in the circulation for a considerable time, administration of repeated doses should lead to an accumulation of the drug in the circulating blood. Animals receiving large doses of khellin showed, after repeated injections, a proportionately greater accumulation of khellin in their blood.

Human subjects were divided into two groups, the first comprising those who received their injection for the first time and the second, those who received daily injection for some days before the collection of the blood samples. The concentration of khellin in the blood was appreciably higher in those subjects who already had repeated injections of the drug.

Khellin is absorbed from the stomach, from the small intestine, and from the large intestine. The absorption from the stomach was studied in anesthetized dogs after complete separation of the pylorus from the duodenum. Absorption from the large intestine was studied only in man. The absorption of khellin from the stomach and especially from the intestine is very rapid. Absorption from the alimentary tract is, therefore, suitable for the maintenance of a high concentration of khellin in the blood, while intramuscular absorption is more suitable when it is desired to raise the concentration of khellin in a short time.

The disappearance of khellin from the tissues is extremely slow and is not related to any particular organ. Its concentration in the blood does not diminish more rapidly than in the tissues.

BELLET.

Küchmeister, H., and Taube, I.: Capillary Permeability in Malnutrition. Ärtzl. Forsch. **1**:278 (Sept. 25), 1947.

Protein content, number of erythrocytes, and volume of packed red cells in venous blood before and after application of an arm cuff at 40 mm. Hg for one-half hour were determined in eleven edematous patients (nine with hunger edema, and two with nephritis) and in fourteen normal subjects (method of Landis and associates: J. Clin. Investigation **2**:717, 1932). From values so obtained, the loss of fluid and of protein in the venous blood after venostasis was calculated. Further, the colloid osmotic pressure of serum was determined in both samples of blood (method of Keys and Taylor: J. Biol. Chem. **109**:47, 1935).

Patients with most marked edema showed the highest losses of fluid and protein (as much as 20.8 per cent and 1.53 per cent). There was, however, no relation between the total protein content in blood and the loss of both fluid and protein after stasis. The colloid osmotic pressure was not always dependent on the total protein content and sank more strongly than did the protein; in 55 per cent of the patients it decreased after stasis, as a result of the escape of proteins (especially of albumin). However, the values of protein content and of the colloid osmotic pressure found in the venous blood after stasis in edematous patients are either within or near normal limits. It must be assumed, therefore, that hunger edema is not only due to hypoproteinemia and to the consecutive fall in osmotic pressure, but also to changes in the capillary walls and in their function.

BRUMLIK.

Hirsch, S.: The Autonomy of the Coronary Circulation. Arch. d. mal. du coeur **40**:433 (Nov. and Dec.), 1947.

The author redescribes the findings of his researches of the past seven years, during which time he has studied histologically the structures contained in the epicardial fat. He found specialized arterioles, the walls of which contained large, clear epitheliod cells and a sphincter-like

arrangement of smooth muscle fibers. The arrangement of the vessels here, especially in the deeper fat at the atrioventricular groove, suggested to him small arteriovenous anastomoses which he compared to glomus bodies. He described a rich network of nerve fibrils and ganglion cells. These anatomical features are offered as a mechanism by which the coronary irrigation is regulated from moment to moment to meet needs of the myocardium.

HECHT.

Vigiu, E., and Pilat, L.: On the Occurrence of an Accentuated First Heart Sound in Incomplete A-V Dissociation With Mitral Stenosis. Arch. d. mal. du coeur **40**:446 (Nov. and Dec.), 1947.

The authors point out that previous explanations of the accentuation of the first heart sound at the apex demanded a short A-V conduction time by postulating the commencement of ventricular systole prior to the time when the mitral leaflets had floated into apposition, the "bruit de Cannon" then being produced by the addition to normal sounds of the sudden shock of mitral closure. A case is presented which the authors believe to be unusual because of the presence of prolonged A-V conduction time. In this instance they explain the accentuated sound by the prolonged period of ventricular filling which held and maintained the valve leaflets in the position necessary for the production of a loud sound. They hold that a "bruit de Cannon" in the presence of prolonged A-V conduction is prima facie evidence of mitral stenosis. Observations are supported and illustrated by simultaneous electrocardiogram, phonocardiogram, and venous and apex pulse tracings.

HECHT.

Burch, G., and Ray, C. T.: Vascular Responses in Man to Ligation of the Inferior Vena Cava. Arch. Int. Med. **80**:587, (Nov.), 1947.

An analysis is presented of twelve female patients in whom the inferior vena cava was ligated for pelvic thrombophlebitis. After ligation of the inferior vena cava, the pressure in the dorsal pedal veins were markedly elevated (from 120 mm. to over 600 mm. of water). A gradual fall in venous pressure occurred with time, but only occasionally did it return to the maximal limits of normal. There was no relationship between the venous pressure and the degree of edema. Section of the lumbar sympathetic nerves did not influence the venous pressure. The paucity or even absence of edema in the lower extremities with considerable elevations in venous pressure made it necessary to re-evaluate the role of hydrostatic pressure in edema formation. Also interesting was the absence of abnormal dilation of the veins of the leg and the feet in the presence of pronounced venous hypertension. In fact, several instances revealed veins of lesser caliber, indicating severe venous spasm. A definite venous hypertension in the superficial low abdominal veins indicated the development of venous collateral flow through these veins and in every instance, the direction of flow was cephalad instead of caudad. Clinical and physiologic observations failed to reveal any detrimental effect from ligation of the inferior vena cava. The circulatory adjustments were adequate, although not all the compensatory mechanisms were clearly understood.

BERNSTEIN.

Hirsch, S., and Zylberszac, S.: Cardiac Infarcts Induced by Excitation and Over-Exertion of Rats. Exper. Med. & Surg. **5**:383 (Nov.), 1947.

The authors believed that the study of the role of the smallest blood vessels in the experimental production of heart muscle damage might require different and more delicate procedures than heretofore used. In searching for such procedures they found that under certain experimental conditions excitation and overexertion of rats produced definite pathologic changes in the heart muscle.

Excitation and overexertion of albino rats were induced by faradization in a specially constructed cage. When the rats were exposed to the faradization, their behavior was very characteristic. One group of animals did not try to avoid the faradization; they moved around in the

cage with signs of fright and excitement until they were unable to stand. The other group of rats developed a kind of protective posture; they crouched in one corner of the cage in such a position that the legs of only one side were in contact with the bottom of the cage. These rats were able to elude faradization for several minutes and were soon so well trained that they assumed their protective position as soon as they were transferred into the cage. Recovery after exhaustion occurred rapidly. All but two animals resumed a standing position a few minutes after the discontinuation of the faradization and started to take food. Eleven rats were exposed to faradization from one to six times.

Depending on the duration of the experiment and the frequency of faradization, increasingly severe changes were found in the heart muscle. The most common early findings were hyperemia of the capillaries and small veins, particularly in the papillary muscles. More striking were the changes of fibrocytes in the interfibrillary tissue of the muscle. These changes occurred as a rule during the first five days and were observed in four of the eleven rats after one to five exposures. In all instances where fibroblast formation and the development of young connective tissue was marked, fragments of disintegrated muscle fibers were found surrounded by connective tissue. The destroyed muscular tissue was eventually replaced by a scar tissue. This was observed in seven of the eleven animals on which this experiment was extended over a period of seven days or more, and after three to six exposures. In five of eleven rats, fully developed lesions were found. These lesions seemed to correspond closely to the histologic picture. In no instance was there any evidence of pathologic change in the branches of the coronary arteries.

BELLET.

Diamondstone, H., Braveman, L., and Baker, A.: Ventricular Tachycardia and Bilateral Amaurosis Produced by Quinine Poisoning. Arch. Int. Med. **80:**763 (Dec.), 1947.

A case is reported of a white man who took a 10 Gm. dose of quinine sulfate, after which he developed ventricular tachycardia, acute coronary insufficiency with electrocardiographic changes, and bilateral amaurosis. Realizing the possibility that quinine produced these changes, this patient was treated as a case of quinine toxicity. The administration of vasodilators resulted in clinical improvement.

The authors believe that the toxic reaction to quinine, and possibly its isomer, quinidine, as demonstrated in this case, was due either to the direct action of the drug on the myocardium and/or to constriction of the coronary artery since constriction of the retinal arteries occurred.

BERNSTEIN.

Merkel, H.: The So-Called Primary Pulmonary Sclerosis. Beitr. z. path. Anat. u. z. allg. Path. **109:**29 (Dec.), 1947.

Eight personal observations are reported and the literature dealing with primary pulmonary arteriosclerosis, pulmonary arteritis, chronic embolism of the pulmonary artery, idiopathic pulmonary arteriopathy, and pulmonary thromboarteritis is reviewed.

All subjects (47 to 76 years of age) were cyanotic and all showed considerable right ventricular hypertrophy. The most important clinical symptoms were cough and dyspnea. The correct diagnosis had not been established during life in any of the eight cases; mitral stenosis or myocardial degeneration was diagnosed wrongly instead. Variable arterioscleroic changes were found in the pulmonary arteries of all subjects; the small arteries and arterioles were involved more extensively than the medium-sized and large arteries. Primary pulmonary arteriosclerosis and pulmonary thromboendarteritis obliterans were the microscopic findings, each in four instances. No importance was ascribed to the coexistent pulmonary emphysema (all cases), chronic bronchitis (three instances), pleural adhesions (three instances), bronchial asthma (one instance).

The microscopic picture resembled that of systemic arteriosclerosis. However, no calcification in the large arteries and no fatty deposits or hyalinization of small arteries and arterioles were

observed. Aside from recent organization of emboli, no signs of inflammation were encountered. The changes in the elastica of the small arteries resembled the "hyperelastosis" of renal arteries. In four instances, endothelial desquamation and formation of fibrinoid thrombi with consecutive narrowing of the lumen were found in the pulmonary arterioles. The common denominator for this angiopathy is an isolated pulmonary arterial hypertension.

In some instances, despite the presence of excessive right ventricular hypertrophy, no changes in the pulmonary vessels were demonstrable. Since it is assumed that an increase in the peripheral resistance must have existed, it is postulated that pulmonary hypertension lacks morphologic manifestation.

BRUMLIK.

Borst, J. R., and Holleman, E. J. W.: Myocardial Infarction Resulting From Intravenous Administration of Hypertonic Solution of Sodium Chloride to Patients With Arteriosclerosis Obliterans of the Lower Extremities. Acta Med. Scandinav. **130**:26, 1948.

Of eighteen patients with obliterating arteriosclerosis of the lower extremities, five were observed during an attack of myocardial infarction. In three of these, treatment with regular injection of hypertonic saline solution may have been directly responsible for the acute episode. In the first patient the attack commenced a few minutes after the infusion had been completed. In the second, an episode of severe vasospasm of the lower extremities occurred shortly after the end of such an infusion. An electrocardiogram taken ten days later revealed unmistakable evidence of subacute myocardial infarction, although no clinical symptoms had occurred at any time and previous electrocardiograms were normal. The third patient complained of increasing dyspnea and angina pectoris during the treatment, which necessitated its termination. Four days following the last treatment, the patient suffered an acute attack of myocardial infarction.

Infusions of hypertonic solution of sodium chloride increases cardiac output and the volume of circulating fluids. It is postulated that in subjects with latent disease of the coronary arteries, infusions of this kind may produce acute coronary insufficiency with resultant myocardial infarction.

HECHT.

Moe, T: A Case of Morgagni-Adams-Stokes Attacks Caused by Transient Recurrent Ventricular Fibrillation Without Apparent Organic Heart Disease. Acta Med. Scandinav. **130**:416, 1948.

This report describes the case of a 38-year-old man who developed attacks of palpitation and who was admitted to the hospital with the typical clinical picture of long episodes of ventricular arrest. Two months after the onset of the earlier symptoms, electrocardiographic examination revealed that these attacks were initiated by a series of ventricular extrasystoles and consisted of long periods of ventricular fibrillation. Sixteen attacks were noted, lasting from 17.7 seconds to 2.5 minutes. Epinephrine was administered before the true nature of the attacks had been discovered. While the patient was under the influence of epinephrine, five spontaneous seizures occurred. Quinidine readily controlled the attacks. No evidence of organic heart disease could be demonstrated.

HECHT.

Borst, J. G. G.: The Maintenance of an Adequate Cardiac Output by the Regulation of the Urinary Excretion of Water and Sodium Chloride; an Essential Factor in the Genesis of Oedema. Acta Med. Scandinav. (Suppl.) **207**:130 1948.

On the basis of a number of clinical observations supported by sodium and chloride balance studies, urea and creatinine clearance values, blood volume determinations, and observations on venous and arterial pressures, it is postulated that a close correlation exists between cardiac output and urinary excretion of water and sodium chloride. As soon as cardiac output declines

to subnormal levels, excretion of sodium chloride and water is reduced. The causes for the decline in output may be gastrointestinal hemorrhage, "shock," early congestive failure, forward failure of the circulation in general, hypoalbuminemia, and cirrhosis of the liver. Raising cardiac output by transfusion, and by digitalization in patients with heart failure and with untreated paroxysmal tachycardia (where an increased minute volume was postulated) resulted in marked retention of water and sodium. This led to an increase in the volume of extracellular fluid, a rise in venous pressure and cardiac output which, in turn, tended to correct the excretory deficiencies.

The author assumes that sodium retention in primarily based on excessive reabsorption of solutes by the renal tubules because little change was noted during the changes in sodium chloride excretion of the creatinine clearance values. The assumption that cardiac output is low in some and high in other syndromes examined was based on the clinical impression and arterial blood pressure determinations. The maintenance of an adequate cardiac output by a renal regulatory mechanism controlling the amount of circulating fluid and venous pressure is repeatedly emphasized.

HECHT.

Jönssen, G.: Visualization of the Coronary Arteries: Preliminary Report. Acta radiol. **29**:536 (June), 1948.

In five of a series of patients in whom aortography was accomplished by rapid injection of contrast medium through a catheter passed up the radial artery into the ascending aorta (Radner, S: Acta radiol. **29**:178, 1948), one or both coronary arteries were visualized. In four instances the tip of the catheter was near the semiluner valves and in one, a few centimeters higher. No attempt was made to study coronary artery anatomy in the roentgenograms which had been aimed at study of the thoracic arterial tree. There was no evidence of heart disturbance, and electrocardiograms before and after the procedure were unchanged. The roentgenograms of three patients are reproduced to show the coronary artery shadows. All three had been studied for patency of the ductus arteriosus. The safety of the procedure as compared with direct intraaortic injection of contrast medium is emphasized.

SAÏEN.

Hansson, C. J., and Jacobsson, E.: The Value of Roentgenography in the Diagnosing of Cardiac Disorder Following Rheumatic Fever. Acta radiol. **29**:541, 1948.

All patients treated for rheumatic fever, or any other conditions commonly falling under this designation, at the Gothenburg Children's Hospital during the period 1922 through 1940 were submitted to a follow-up examination with a view to gaining some idea of the prognosis in this disease as it is seen in Sweden. The heart of each patient was submitted to a thorough physical examintion, both under resting conditions and after exertion, and an electrocardiogram was also made in each case. Roentgen examination of the heart was then carried out.

The roentgenologist was told only that the patient in question had had a rheumatic infection, and, therefore, was not influenced during his studies by any findings that might have been made by physical examination. During the course of the investigation clinician and roentgenologist met for discussion and comparison of their findings in each individual case.

In 297 cases, (60.1 per cent) there was complete agreement between the clinical and roentgenographic findings. There was no agreement in 170 cases (39.9 per cent). It is also of interest to note that in no less than 150 cases the clinical examination revealed unequivocal evidence of organic heart disease, whereas the roentgen examination brought out nothing in this respect. In 387 cases (78.3 per cent), the roentgen examination was of no particular significance in the diagnosing of organic heart defects, since organic involvement could be established beyond all doubt by physical examination alone. In the remaining 107 cases (21.7 per cent), the roentgenogram was the decisive factor in the diagnosis.

BELLET.

Book Reviews

DIAGNOSTICO DAS FORMAS ANATOMO-CLINICAS DA CARDITE REUMATICA. By E. Magalhães Gomes, M.D. Rio de Janeiro, 1947, Rodriguez and Co., 345 pages and 65 figures.

This book is a comprehensive study of rehumatic disease with special regard to rheumatic carditis. The disease is considered to be an infectious process with allergic reactions to the proteins of *Streptococcus hemolyticus*.

The diagnosis of the disease is studied with particular attention. Among the laboratory data, the Weltmann reaction is considered to be very accurate, a conclusion which should be accepted with reserve. The various possible complications of rheumatic disease are studied in detail. These include renal, pleuropulmonary, hepatic, thyroid, ocular, and neurological disturbances. The study of cardiac manifestations is completed by the description of clinical cases and the presentation of excellent electrocardiographic, phonocardiographic, and roentgenologic documentation.

This monograph should find its place in the library of all centers for the study of rheumatic fever.

A. LUISADA, M.D.

LA PATHOGENIE DES ALTERATIONS ELÉCTROCARDIOGRAPHIQUES DE LA PÉRICARDITE. By E. Coelho, M.D. Lisbon, 1947, Bertrand, Ltd., 74 pages and 58 figures.

This mongraph reports studies of the electrocardiograms in 138 cases of pericarditis. These include examples of uremic, tuberculous, purulent, and rheumatic types; hemopericardium and calcific and constrictive pericarditis are also studied.

Only six cases presented a normal electrocardiogram; in all others electrocardiographic changes were observed, at least in certain phases of the disease. The diagnostic value of the electrocardiogram was found to be high; in certain cases, fever and electrocardiographic changes were the only signs, and paracentesis of the pericardium confirmed the diagnosis. According to the author, there is no single type of electrocardiographic change and no typical evolution.

The electrocardiogram is of no help in making an etiological diagnosis. However, upward displacement of RS-T segment with high take-off of the T wave was found only in purulent and rheumatic pericarditis and never in tuberculous pericarditis. The deeply inverted T wave, encountered in certain cases of uremic pericarditis, is considered as a pre-existing change and sometimes the result of high potassium content of the blood.

In certain cases of associated rheumatic pericarditis and associated myocarditis, the electrocardiogram may contribute to the etiological diagnosis.

The evolution of the electrocardiogram varies in each type of pericarditis; the changes may persist indefinitely in cases of constrictive pericarditis. The most transient changes are observed in rheumatic pericarditis; in this type the changes may disappear within a few days unless constrictive pericarditis develops. In uremic pericarditis, the electrocardiographic changes are permanent. In purulent pericarditis, normalization of the tracing coincides with healing of the form, while persistence of the changes indicates constrictive evolution. Irritation of the pericardium due to hemorrhage causes changes which disappear after elimination or adsorption of the effusion. According to the author, complete evolution of the electrocardiographic changes, from the upward RS-T displacement to the inversion of the T wave in all leads, rarely is observed.

The author feels that neither myocardial anoxemia nor myocardial lesions explain the electrocardiographic alterations. These are due to irritation of the epicardium followed by bioelectric changes.

This extremely valuable monograph presents the protocols and documents of selected interesting cases and certainly will be quoted extensively in the future.

A. LUISADA, M.D.

LA PRESSION DE LA ARTERIA PULMONAR. By V. A. J. Alberti, M.D. Buenos Aires, 1948, El Ateneo, 170 pages and 40 figures.

A detailed study is made of the various experimental devices by which pulmonary artery pressure can be measured in animals. This is followed by several chapters discussing the effects

on pulmonary artery pressure of respiration, pulmonary embolism, pneumothorax, various reflexes, and various drugs. The last two chapters are devoted to the study of normal pulmonary pressure in man. Two methods are examined in particular: first, that of direct puncture of the artery through the chest wall, a technique devised by the author; and second, that of catheterization of the pulmonary artery.

The personal experience of the author with the various technical procedures is reported. For this reason and for the extensive bibliography, the book should prove to be valuable for students of the subject.

A. LUISADA, M.D.

DOENÇAS CARDIO-VASCULARES. By F. S. Laranja, M.D., and co-workers. Rio de Janeiro, 1948, Editora Cientifica, 733 pages and 215 figures.

This book is a volume in the collection of *Pathology and Therapeutics* by Struempell. The work of the old German clinician has been completed and revised by several Brazilian cardiologists under the direction of Dr. Laranja who has contributed most.

While the book suffers somewhat from its mixed origin, the knitting of old and new parts has been accomplished with skill. Many chapters are entirely new and among them is a valuable study of the cardiac lesions in Chagas' disease.

The book includes the following main divisions:

I. Etiological Factors of Cardiac Diseases.
II. Anatomical Changes of the Heart and Vessels.
III. Vascular Syndromes of the Heart.
IV. Functional Cardio-Vascular Disturbances and Treatment.

This scheme has the disadvantage of repetition. However, the concise form of the text partly compensates for it. Certain chapters seem out of proportion to others, but this can be explained by the importance that the diseases discussed in those chapters have in Brazil.

The documents presented are excellent; the sketches, clear. The binding of the book is first class while the paper varies from adequate to good.

A. LUISADA, M.D.

VASCULAR DISEASES IN CLINICAL PRACTICE. By Irving Sherwood Wright, M.D., Associate Professor of Clinical Medicine, Cornell University Medical College; Chief of Section on Vascular Diseases of the Department of Medicine, New York Hospital. Chicago, 1948, The Year Book Publishers, Inc., 514 pages and 104 figures. Price $7.50.

I know of no small book that offers such concise and practical information on a subject that is not too well taught even now in medical schools. The author is an outstanding authority on vascular diseases, and one who knows how to impart his knowledge to others. This reviewer has no criticism to make either as to the content of the text or the format. The author shows how any physician can diagnose and treat the diseases dealt with. After a chapter on classification and one on methods of study of the patient, individual diseases are discussed. It is to be hoped that the author will keep his book alive for many years by revisions as they may be indicated.

WALLACE M. YATER, M.D.

TONOSCILLOGRAPHY AFTER EXERCISE. By Borje Ejrup, Med. Lic. Stockholm, 1948, Svenska Tryckeriaktiebolaget, 285 pages and 51 figures.

Dr. Ejrup presents a very complete monograph in an adequate English translation in which he discusses the instrument he demonstrated in 1943 for the automatic recording of peripheral arterial oscillations, and its use in intermittent claudication and a few related conditions.

The instrument which this author has devised is a very ingenious one for taking rapid, repeated oscillometric readings at regular intervals. The instrument accomplishes this automatically and makes a recording that does not have any subjective error.

The instrument automatically inflates (from tanked gas) a recording cuff to 50 mm. Hg and then inflates the proximal pressure cuff, gradually increasing the pressure as high as is needed,

and then releases the pressure in both cuffs. Another complete cycle is begun thirty seconds after the start of the first. The pressure cuff is connected to a lever which rises on a stationary drum and records the pressure at all times in a vertical line. Meanwhile the pulsations are recorded by horizontal deflections of the same needle. The drum moves 2.0 cm. at the close of each recording and is ready for another tracing. The result of this is a series of tracings from which both the systolic and diastolic blood pressures can be estimated and the amount of oscillations at the various tensions are a matter of permanent record. These are similar to the oscilometric readings which are usually taken, but they are recorded rapidly, frequently, and automatically. The machine is adaptable for either the one- or two-cuff method. Measurement of the oscillations can be made by having a standard amplification and by direct measurement of the swing, or by adjusting the maximal swing to a fixed amount and then by measuring the amplification required. While the latter method is preferable from theoretical considerations, it does introduce considerable subjective error and the necessity of a notation of the amplification, whereas the former is purely objective.

The fact that the tracings are taken fequently, rapidly, and automatically makes it possible to trace the degree of pulsations of the arteries immediately after exercise and to follow changes and recovery for as long as desired.

The author has very carefully checked so-called normal subjects and their responses to exercise. The normal subjects included postmen, dancers, football players, office workers, elderly subjects, and convalescents from nonrelated illnesses; none of the normal subjects showed evidence of vascular diseases. The author has shown that the normal reaction after standardized exercise is an increase in the systolic and diastolic blood pressures and in oscillations which lasts for a few minutes.

One cannot help but be impressed with the lengths to which Dr. Ejrup went to get a standardized procedure with many variables controlled and with the documentation of all subjects. Controls were checked with a complete physical examination, including palpation of all arteries, sedimentation rate, electrocardiograms before and after strenuous exercise, and fluoroscopy.

The differences obtained in the controls were a matter of degree and were reproducible in the same subject at different times. There was less variation after exercise than before. The explanation was offered that after exercise there was a measurement of the full capacity of the arterial system, whereas at rest the vessels might be in equilibrium at any point.

In patients with intermittent claudication there is a definite drop of blood pressure in the affected limb and a diminution of pulsations after exercise lasting from one and one-half to over twenty minutes. This premise was developed from thirty-four cases in which diagnoses of arteriosclerosis obliterans were confirmed by complete physical examination, including retinoscopic venous pressure, Decholin circulation time, electrocardiogram before and after hypoxemia and exercise, Nylin's function test, soft tissue x-ray films, complete blood count, sedimentation rate, cholesterol and total lipids, measurement of skin temperature before and after sympathetic block or tetraethylammonium chloride, and the reactive hyperemia test. In all the cases there were direct arteriographic x-ray studies which were correlated with the oscillograms.

Excellent quantitative correlation was noted between the degree of block and the localization of block in the arteriograms and the oscillograms. In 119 cases of definite proved intermittent claudication without arteriograms, there was comfirmatory evidence of blocks in the arteries, whereas in 455 cases with symptoms in the legs not believed to be of arterial origin the oscillograms were normal. Several cases were followed over several years with the exercise oscillograms paralleling the clinical course very closely.

There are also a few cases of Raynaud's phenomenon in which there were normal oscillograms before and after exercise. The author feels that this instrument is adequate for distinguishing organic disease from vasospastic disease, although he admits his series of vasospastics is still far too small. The reviewer believes that the evidence regarding this point is not conclusive.

There is an extremely interesting chapter on coarctation of the aorta. Twenty-six cases were studied after the resection of the stricture with end-to-end anastomosis of the aorta performed by Dr. Crafoord.

IRVING S. WRIGHT, M.D.

ELEKTROPHYSIOLOGIE. I. BAND: ALLGEMEINE ELEKTROPHYSIOLOGIE. II. BAND: SPEZIELLE ELEKTROPHYSIOLOGIE. By Hans Schaefer, M.D. Vienna, 1942, Lithoprinted by Edward Brothers, Inc., Ann Arbor, Mich., 1944, 44 pp. and 99 figures.

The author, the Director of the Department of Experimental Medicine of the once famous Kerckhoff Institute in Bad Nauhaim, Germany, has set himself a task that appears almost impossible of achievement. Without the usual staff of coeditors usually requisitioned for such undertakings, he ranges in these two volumes over the entire field of electrical properties of living tissues, exclusive of plants. Upward of twelve thousand references are cited covering 172 pages of fine print. This alone establishes the two volumes as an important guide book to anyone interested in fundamental approaches to medicine.

The book appeared in Germany during the war and to the reviewer's knowledge the original plates were soon destroyed. The only copies now available are those of the lithoprinted edition of the Edwards Brothers, published in 1944 by the Alien Property Custodian.

The first volume deals with general aspects of electrophysiology. It covers the passive electrical properties of living tissue, such as resistance, capacitance, polarization, and electrotonus. There follows a general discussion of the electrical response of tissue to external stimulation which includes a section on the excitability of individual tissues and organs in various species and quantitative data on Lapicque's rheobase and chronaxia. A chapter on the phenomenon of "local excitatory disturbance" (change in excitability during constant current application) leads to an extended discourse on the nature of action currents, resting currents, and injury currents (cell, skin, nerve, muscle). A chapter on transmission of excitation from organ to organ and one on the influence of poisons on the electrical properties of muscle and nerve complete the text of the first volume.

The second volume deals specifically with the electrophysiology of cardiac muscle, skeletal muscle and nerve, and with the electrical properties of sensory organs and of the central nervous system. A section on the electrophysiology of the skin and a chapter on the electrical phenomena of electrical fishes is appended.

Where the reviewer is able to critically evaluate the text, the occasional omission of pertinent references is unfortunate as the strength of the book is based to a large though by no means exclusive extent on the citation of the work of others and on its extensive reference section. It illustrates that the scope of the presentation begins to exceed the capacity of one single mind and that a joint authorship would perhaps have provided an even more comprehensive account. As an example may be cited the section on the electrophysiology of the heart muscle which serves well as an introductory guide to certain basic concepts. It cannot, however, be regarded as a final source book comparable, for instance, to the earlier and in scope much more limited volumes by Lewis and by Wenckebach and Winterberg. The author's preoccupation in this section with Schütz's and Schellong's debatable differential theory of the electrocardiogram serves to detract somewhat from an otherwise excellent presentation. It is gratifying to find that the ubiquitous role of the electrical responses of tissues as a primary phenomenon in general physiology is repeatedly emphasized throughout the book.

In spite of the slightly overponderous scientific German, the volumes represent an important, unique, and, with minor exceptions, successful distillation of the subject. The external appearance of the lithoprinted edition could be greatly improved.

H. H. HECHT, M.D.

ILLUSTRATIVE ELECTROCARDIOGRAPHY, 3rd Edition. By Julius Burstein, M.D., and Nathan Bloom, M.D. New York, 1948, D. Appleton-Century Co., Inc., 309 pages, 99 plates, 23 figures. Price $6.00.

This book presents the rudiments of electrocardiography, phonocardiography, and radiology of the heart in a simple, concise manner and is so illustrated as to be understandable to the beginner in this field. Discussion of the material presented is brief. Controversial issues are avoided. A chapter on precordial and augmented leads is included. The authors, in nearly every instance, illustrate the subject discussed with an electrocardiogram showing all leads, rather than simply showing one lead, as is often done.

This is a well-arranged, elementary book designed for the beginner in this field.

JOSEPH A. WAGNER, M.D.

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CARDIOVASCULAR REGISTRY OF PATHOLOGY

The first meeting of the Advisory Committee, with Dr. Wallace M. Yater as Chairman, was held in the Army Institute of Pathology, Washington, D. C., on Friday, Jan. 28, 1949. The entire Committee, Jesse E. Edwards, Jane Sands Robb, Joseph T. Roberts, and Helen B. Taussig, was present. General Raymond Dart, Director of the Institute, and Colonel James E. Ash, Scientific Director of the American Registry of Pathology, were also present.

This Cardiovascular Registry is sponsored by the American Heart Association for the following purposes:

1. The accumulation and maintenance of collections of pathologic materials and related case records.
2. The provision of consultation service for pathologists.
3. The preparation of teaching material in such forms as may be most readily and satisfactorily available for loan to qualified physicians, investigators, or students.
4. The establishment of facilities for the training of students and fellows in pathology.
5. To facilitate the accessibility of the materials in the Registry for students and qualified investigators who may be authorized to make definitive researches based on Registry material.

At its first meeting, the Committee voted to limit the collection of material to the following items:

1. Cardiovascular anomalies.
2. Subacute bacterial endocarditis.
3. "Collagen system diseases," particularly polyarteritis nodosa and disseminated lupus erythematosus.
4. Tumors of the heart and vascular system.

In addition, any interesting or unusual case is desired, particularly if a well-documented case report is available.

Cases may be submitted for consultation, but it is preferred that such cases be first examined by a local pathologist.

Special, simplified forms will be available shortly to facilitate the submission of clinical data.

All members are requested to cooperate so that the Cardiovascular Registry can be developed and can contribute to education and research in this field. Additional information can be obtained from the Director, Army Institute of Pathology, Washington 25, D. C., or from the American Heart Association.

VITAL STATISTICS

Figures on the causes of death in 1947 have been released by the National Office of Vital Statistics of the United States Public Health Service. Cardiovascular disease leads as the cause of death, with 626,176 fatalities in 1947 against 588,451 in 1946. The breakdown of the 1947 figure is as follows:

Diseases of the heart	460,580
Intracranial lesions of vascular origin	131,039
Acute rheumatic fever	1,024
Other diseases of the circulatory system	33,533
	626,176

Comparison of the total with deaths from other causes is as follows:

	1947	*1946*
Cardiovascular diseases	626,176	588,451
Cancer	189,811	182,005
Accidents	99,579	98,033
Nephritis	80,288	81,701
Pneumonia	61,836	62,324
Tuberculosis	48,064	50,911

1949 NATIONAL CAMPAIGN

Specific results of the 1949 Campaign cannot be reported until a later issue of the *Journal*. In general, satisfaction was felt with advance preparation for the drive, and the task of reaching the $5,000,000 goal was tackled with enthusiasm.

The theme of publicity and educational material was one of optimism and encouragement. This was echoed in the statement of President Truman and in the proclamations and statements of many of the State Governors. Newspapers, magazines, radio, and television all cooperated generously in carrying the message of hope rather than fear.

Radio Promotion

Opening day publicity was highlighted by an American Broadcasting Company radio network broadcast which heard addresses by Dr. Tinsley R. Harrison, President, and Harold E. Stassen, National Chairman. On the same date, Dr. Leonard A. Scheele, Surgeon General of the United States Public Health Service, spoke over the Mutual network.

Throughout the campaign period and just previous to it, numerous radio programs were devoted exclusively to the subject of heart disease or the campaign. These included an American Broadcasting Company network presentation of the history of the Association by Ted Malone; dramatic shows on all four networks dealing with rheumatic fever, high blood pressure, and other heart problems; a National Broadcasting Company round-table discussion; and talks by committee chairmen, including Maurice J. Tobin, United States Secretary of Labor, who is Chairman of the National Labor Committee.

Precampaign estimates were that almost without exception all sponsored network radio shows would devote commercial time to educational information or an appeal for funds. In addition, spot announcements were expected from nearly all of the 2,000 radio stations in the country; all but a few score requested kits and transcriptions for use.

Of major importance was the "Truth or Consequences" program conducted by Ralph Edwards and sponsored by Procter and Gamble. The "Whispering Woman" contest on this program was introduced on January 15.

Campaign Committees

Officially recognized campaign committees were organized in a great number of communities to conduct fund-raising and educational programs during the National Campaign in February. Most of these were under the sponsorship of existing local heart associations. Others represent potential local associations or chapters of state-wide associations.

The following is a partial list of cities where such campaigns were conducted. It does not include several hundred communities where committees were independently organized through joint enterprise of civic groups like the American Legion, Rotary, Lions, Kiwanis, and other public-spirited organizations:

Atlanta, Ga.
Austin, Texas
Baltimore, Md.
Binghamton, N. Y.
Birmingham, Ala.
Boston, Mass.
Bridgeport, Conn.
Buffalo, N. Y.
Charleston, W. Va.
Charlotte, N. C.
Chattanooga, Tenn.
Chicago, Ill.
Cleveland, Ohio
Columbia, S. C.
Columbus, Ohio
Cumberland, Md.
Dallas, Texas
Des Moines, Iowa
Detroit, Mich.
Fort Worth, Texas
Grand Rapids, Mich.
Hartford, Conn.
Houston, Texas
Indianapolis, Ind.
Jersey City, N. J.
Kansas City, Mo.
Memphis, Tenn.
Miami, Fla.
Milwaukee, Wis.
Minneapolis, Minn.
Nashville, Tenn.
Newark, N. J.
New Haven, Conn.
New Orleans, La.
New York, N. Y.
Peoria, Ill.
Philadelphia, Pa.
Portland, Ore.
Richmond, Va.
St. Louis, Mo.
St. Paul, Minn.
San Antonio, Texas
Seattle, Wash.
Springfield, Mass.
Syracuse, N. Y.
Trenton, N. J.
Tulsa, Okla.
Washington, D. C.
Wheeling, W. Va.
Wilmington, Del.
Winston-Salem, N. C.
Worcester, Mass.
Youngstown, Ohio